"ROLE OF BRONCHOSCOPY IN DIAGNOSIS OF PULMONARY INFECTIONS IN NON-HIV IMMUNE COMPROMISED HOST"

Dissertation submitted to The Tamil Nadu Dr. M.G.R. Medical University in partial fulfilment of the requirements for the degree of

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Branch – XVII

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BONAFIDE CERTIFICATE

This is to certify that the dissertation titled **"ROLE OF BRONCHOSCOPY IN DIAGNOSIS OF PULMONARY INFECTIONS IN NON-HIV IMMUNE COMPROMISED HOST"** is the Bonafide work done by **Dr. PALANIAPPAN C** during his M**.D (Tuberculosis and Chest Diseases)** course in the academic years 2014-2017, at the Institute of Thoracic Medicine and Rajiv Gandhi Government General Hospital – Madras Medical College, Chennai. This work has not previously formed the basis for the award of any degree.

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CONTENTS

ROLE OF BRONCHOSCOPY IN DIAGNOSIS OF PULMONARY INFECTIONS IN NON-HIV IMMUNE COMPROMISED HOST

INTRODUCTION

The immune compromised host is defined as a person who has an alteration in phagocytes, the humoral or cellular immunity that increases the risk of infectious complication [1]. There is a growing group of individuals apart from ACQUIRED IMMUNODEFICIENCY SYNDROME (AIDS) who are now immune suppressed like, those receiving immune suppressants for Solid Organ Transplants (SOT), Bone Marrow Transplant (BMT), Connective Tissue Diseases or treated with chemotherapeutic agents for cancer. Widespread use of "Biological Agents", which are generally antibodies targeting specific cell type or pathway of inflammation, has further expanded the susceptible population.

Managing systemic infections are challenging in such patients among which pulmonary infection is very frequent. The development of pulmonary disease among such patients is considered as a serious problem. The differential diagnosis includes infectious and many non-infectious causes. *Given the broad spectrum of potential infections and non-infectious causes, coupled with inherent toxicities of many therapies, a specific microbiological and cytopathological diagnosis should be considered essential to the management of pulmonary infections in non-HIV immune compromised host* [2]

Noninvasive test available can be done easily with less risk, but overall they are of little diagnostic use and their yield is also low. So invasive strategies become essential for management of pulmonary diseases. Among the invasive test Bronchoscopy and Bronchoalveolar Lavage (BAL) has proved to be the procedure with good yield and is well tolerated even in critically ill patients, with

a low complication rate. It also leads to the most appropriate diagnosis. The sensitivity and specificity for diagnosing pulmonary infections is also good. Early diagnosis and appropriate treatment reduces the mortality and increases survival benefits. Hence, early bronchoscopy if possible before starting antibiotic therapy remains crucial in the management of immune compromised host with pulmonary infections.

REVIEW OF LITERATURE

The immune compromised host is defined as a person who has an alteration in phagocytes, the humoral or cellular immunity that increases the risk of infectious complication or an opportunistic process like lymphoproliferative disease or cancer [1]

J.L.Mahon et al[3]., defines an immunocompromised patient is one with any defect in the immune system and immunodeficiency is applied to any person affected by disease or situations in which the immune system itself, including complement, phagocytes and lymphocytes is impaired

CENTER FOR DISEASE CONTROL (CDC) [4] for practical purposes, divides immune compromising conditions into 3 broad categories

A. Persons who are severely immune compromised not as a result of HIV infection;

B. Persons with HIV infection; and

C. Persons with conditions that cause limited immune deficits (e.g., asplenia, renal failure)

SEVERELY IMMUNOCOMPROMISED, NON-HIV-INFECTED PERSONS [4]

1. Congenital immunodeficiency
2. Leukemia, lymphoma, generalized malignancy

3. Therapy with alkylating agents, antimetabolites, radiation, or large amounts of corticosteroids

MEDICAL CONDITIONS THAT CAUSE LIMITED IMMUNE DEFICIENCY [4]

1. Renal failure - End stage renal disease is associated with infections which contribute to 20% mortality, which is due to alteration in immune system[5] Matthias Girndt et al [6]., in his article on the impaired cellular immune function in patients with end-stage renal failure states that patients with chronic renal failure are at increased risk of infections similar to other acquired immune defects. The secondary immune failure is due to uremic intoxication per se and by altered renal metabolism of immunologically active proteins.
2. Alcoholic cirrhosis
3. Asplenia

The **IDSA**[7] (**INFECTIOUS DISEASE SOCIETY OF AMERICA**) has defined immune suppression as High & Low level immune suppression.

HIGHLEVEL IMMUNOSUPPRESSION INCLUDES:

1. Combined primary immunodeficiency disorder (eg, severe combined immunodeficiency)
2. Receiving cancer chemotherapy
3. Within 2 months after solid organ transplantation

4. With HIV infection with a CD4 T-lymphocyte count <200 cells/mm3 for adults and adolescents and < 15% for infants and children
5. Receiving daily corticosteroid therapy with a dose ≥20 mg (or >2 mg/kg/day for patients who weigh <10 kg) of prednisone or equivalent for ≥14 days
6. Receiving certain biologic immune modulators, that is, a tumor necrosis factor-alpha (TNF-α) blocker or rituximab

LOW-LEVEL IMMUNOSUPPRESSION INCLUDES:

1. Asymptomatic HIV-infected patients with CD4 T-lymphocyte counts of 200–499 cells/mm3 for adults and adolescents and 15–24 % for infants and children
2. Those receiving a lower daily dose of systemic corticosteroid than for high-level immune suppression for ≥14 days or receiving alternate-day corticosteroid therapy
3. Those receiving methotrexate (MTX) ≤0.4 mg/kg/week, azathioprine ≤3 mg/kg/day, or 6-mercaptopurine ≤1.5 mg/kg/ day

ETIOLOGY AND DIFFERENTIAL DIAGNOSIS FOR PULMONARY DISEASES IN NON-HIV IMMUNE SUPPRESSED

Includes both infectious & non-infectious etiologies.

Rañó A et al [8]., in his study of pulmonary diseases in non-HIV immuno compromised patients found that 77% of pulmonary diseases were infectious and remaining 23% were non-infectious and among non-infectious causes pulmonary edema and alveolar haemorrhage were most common.

Similarly, Rosenow EC, et al [9]., observed the same differential diagnosis for pulmonary diseases among non-HIV immunocompromised host. In his study he observed 25% of pulmonary diseases were due to non-infectious causes.

Bianca Harris et al [10]., in his focussed review on Bronchoscopy in Solid Organ and Haematopoietic transplant patients observed the following differential diagnosis for pulmonary diseases.

Table 1. Differential diagnosis of pulmonary disease in non-HIV immuno compromised host [10,11]

1. Infection	7. Acute rejection
2. Drug induced pulmonary disease	8. Malignancy
3. Recurrence of underlying disease	9. Pulmonary edema.
4. Pulmonary haemorrhage	10. Combination of above
5. Idiopathic fibrosis	
6. ``Unrelated'' disease	

PULMONARY INFECTIONS IN NON-HIV IMMUNOCOMPROMISED

Infections are the most common cause of pulmonary diseases. An unilateral, localized process is very likely to be infectious in origin (90%), whereas diffuse disease is somewhat less frequent (75%) [12,13,14]

Nimrod Maimon et al [11]., approaches the differential diagnosis of pulmonary infections in two ways, first is to relate the various organisms to defect in primary immune system, the more important second one is to consider the probability of

various organisms in context of different underlying immune defect[11]. According to him the pathogens summarized below account for 90% of opportunistic infections. [11]

Table 2. The most common infectious organisms [11]

Bacteria	**Fungi**	**Viruses**	**Protozoa**
Staphylococcus Aureus	Pneumocystis carini	Cytomegalovirus	Toxoplasma gondii
Streptococcus pneumoniae	Candida sp.	Herpes simplex	Strongyloides stercoralis
Staph. epidermidis	Aspergillus sp.	Herpes zoster	
Pseudomonas aeruginosa	Histoplasma capsulatum	Respiratory syncytial virus	
Escherichia coli	Blastomyces dermatitidis	Influenza A	
Legionella	Coccidioides immitis	Enterovirus	
Nocardia	Cryptosporidium neoformans		
Mycobacteria sp.			

Bacterial, fungal, viral, and mycobacterial pathogens may infect the lungs of immunosuppressed patients. In a prospective series by Rano et al [8]., among 200 non-HIV immunocompromised patients, infectious agents were recovered from more than three fourth of subjects. An etiological diagnosis was obtained in 81% with 19% no diagnosis. Among the 81%, infections were 77% and non-infectious causes contributed to 23%. Among infections bacterial was predominant with

23%, followed by fungal with 17% and viral with10% [8]. According to Andrew F. Shorr, MD et al.,[15] the most common bacterial organisms are nosocomial organisms like Pseudomonas and MRSA. Aerobic Gram-negative bacilli such as Klebsiella pneumonia may also lead to pneumonia

SPECTRUM OF PULMONARY FUNGAL INFECTIONS

Aspergillus infection remains the most common cause of fungal pneumonia [15]. *Aspergillus* species have emerged as important causes of morbidity and mortality in immunocompromised patients [16]. Among the Aspergillus species, Aspergillus fumigatus is the most common species recovered [17].

Paterson DL, et al.[12] found Aspergillus infection occurs in 1 to 8% of patients undergoing various solid organ transplants (SOTs) and Hematopoietic stem cell transplants (HSCTS). Chest pain, dyspnea, and hemoptysis are the classical presenting symptoms. Some patients initially have no symptoms.

Jantunen et al [13] in his series on invasive and probable fungal infections among bone marrow transplant recipients observed Aspergillus was the most frequent cause and only 50% had chest symptoms, 32% had fever and remaining were asymptomatic. The triad of symptoms of chest pain, hemoptysis, dyspnea can occur in pulmonary embolism leading on to confusion in diagnosis. The chest radiograph may initially be normal in upto 10% of cases.[12] Hence, early use of CT scan is necessary [12]. An area of low attenuation may arise next to areas of consolidation referred as halo sign. But it is not specific and is also a late finding[12]. Infections due to other angioinvasive filamentous fungi, such as

Zygomycetes, *Fusarium* species, and *Scedosporium* species, as well as to *Pseudomonas aeruginosa* and *Nocardia* species, may cause a halo sign.[16]

Calliot D, et al [14]., in his study of definitive Aspergillus cases, the sensitivity of halo sign was only 50%. The yield of bronchoscopy for aspergillosis in immune suppressed patients is approximately 50%

FREDERICK W. KAHN et al [18]., in his study of 82 immunocompromised patients undergoing bronchoscopy for pulmonary infiltrates found that Aspergillus hyphae was found 9 out 17 cases with invasive aspergillosis. BAL had a sensitivity of 53% and specificity of 97% and positive predictive value of 75% as per his study. Thus he concluded that BAL was a valuable procedure for diagnosing invasive aspergillosis. The newer techniques like galactomannan assay has sensitivity 80-90% and specificity > 95%.[19,20].

The other important fungi that cause pneumonia in immunocompromised patients are endemic mycosis Histoplasma capsulatum, Coccidioides immitus, and Blastomyces dermatitidis [15].

Candida though often isolated from respiratory tract of immunocompromised patients rarely cause pneumonia except in lung transplant recipients [15]. Haron E et al [21]., in his study identified primary candida pneumonia in only 0.4% of autopsies at the M.D. Anderson Cancer Center. Since the isolation of Candida often represents colonization rather than true infection attributing pulmonary infiltrates to Candida pneumonia is difficult. Demonstration of tissue invasion by transbronchial or surgical lung biopsy is required for definitive diagnosis. But

even though Candida is frequently a colonizer, Respiratory tract Candida colonization is associated with worse clinical outcomes and is independently associated with increased hospital mortality [22,23].

PNEUMOCYSTIS CARINII PNEUMONIA

Yale SH, et al [24]., found in his study up to 90% of Pneumocystis carinii pneumonia occur in patients treated with steroids within 4 weeks of diagnosis. He found the mean corticosteroid dose was 30mg/day and mean duration of steroid therapy was 12 weeks before the development of pneumonia.

Pneumocystis carinii pneumonia also has been linked directly to Fludarabine therapy for CLL [25]. The radiological pattern tends to be bilateral with fine Perihilar or small nodular infiltrates.

BAL has a very good yield for PCP. The BAL yield for PCP with conventional stain is 80% in non-HIV & 95% in HIV patients [26]

PREVALENCE OF PULMONARY TUBERCULOSIS

The incidence of tuberculosis varies depending on the underlying cause for immunosuppression. In areas where Tuberculosis is highly prevalent the possibility of tuberculosis is high.

Jane C. Chan et al.[27], in his study in Hong Kong among 62 Non-HIV immunocompromised found that tuberculosis was the second most common cause of pulmonary infections after bacterial infections. The incidence of tuberculosis was 19%. The overall bronchoscopic sensitivity for tuberculosis

was 91%. The radiographic presentation was nonspecific. Hence in countries where there is high prevalence of tuberculosis, bronchoscopy should be utilized readily for smear negative cases in immunocompromised patients and empirical treatment may be started awaiting culture results [27]

NON-INFECTIOUS ETIOLOGIES

There are various non-infectious causes of pulmonary diseases in immunocompromised. Upto 25% of pulmonary diseases in immunocompromised can be attributed to non-infectious causes [8,28]. Some of the non-infectious causes can have a poorer prognosis.

PULMONARY EDEMA

Pulmonary edema is one of the common non-infectious causes of pulmonary disease. Andrew F. Shorr et al[15]., states that the

Causes of pulmonary edema include,

1. Hydration prior to chemotherapy for leukemia.
2. Volume overload status in chronic kidney disease patients and sometimes post renal transplant patients.
3. Chemotherapeutic agents like doxorubicin induced cardiotoxicity.
4. Indirect causes like drugs, radiation, sepsis, that promotes lung injury and capillary leak.

Patients have diffuse pulmonary infiltrates predominantly involving lower lobes and are afebrile. Some patients can even decompensate quickly, but respond to

treatment well and the prognosis is good. Hence extreme care needs to be taken while assessing the fluid status of immunocompromised patients. [15]

RECURRENCE OF UNDERLYING DISEASE [15]

In patients with underlying malignancy the disease progression may result in the development of pulmonary disease. The infiltrates may be discrete nodules, masses, diffuse alveolar infiltration as seen in lymphomas or lymphangitic pattern with interstitial involvement may also occur. Bronchoscopy helps to rule out infections and helps to get the tissue biopsy needed to prove the diagnosis.

DRUG INDUCED PULMONARY DISEASE [15]

Many drugs are associated with pulmonary toxicity. Some like Busulfan are directly implicated in causing pulmonary disease. Pathological patterns of drug induced lung disease may be in the form of diffuse alveolar damage (DAD), granulomatous reactions, and nonspecific pneumonitis [28]. The diagnosis of drug induced lung damage is made clinically,

1. The temporal relationship between the use of a particular agent and the subsequent development of symptoms
2. Improvement in pulmonary function after withdrawal of the agent
3. Exclusion of infection

Some common drugs associated with pulmonary toxicity include Busulfan, Cyclophosphamide, Methotrexate, Azathioprine, Bleomycin etc... [15,28]

RADIATION INDUCED LUNG INFILTRATES [2]

Radiotherapy for malignancies can involve the lungs. They result in acute pneumonitis or more slowly, progressive pulmonary fibrosis. Following a dose of radiation to the lungs >2000 rads, radiation injury may be seen. The acute form of radiation pneumonitis may present as bronchitis or esophagitis, with dry cough, fever, fatigue, hypoxemia, and dyspnea that develop over 6 to 12 weeks. Radiation fibrosis usually occur in 6 to 9 months, and pulmonary function may take upto 2 years to plateau. Radiation injury may follow a unique pattern on CT chest. The lesions are sharply defined and bounded. They do not follow the anatomic border.

DIFFUSE ALVEOLAR HAEMORRHAGE

Diagnosed by bloodier return from BAL and the presence of hemosiderin laden macrophages. If 20% of the alveolar macrophages are hemosiderin laden, then DAH is present [29]. Radiography shows diffuse alveolar infiltrates in middle and lower lung fields. The incidence ranges from 2 to 14% [29]. The pathogenesis of DAH is unclear. DAH likely arises following an initial lung injury from either chemotherapy or irradiation that results in endothelial damage [29,30]. Treatment consists of high-dose corticosteroids. Dosages used have ranged from 500 mg to 2 g per day of IV Methylprednisolone [29,30]

MORBIDITY AND MORTALITY OF PULMONARY INFECTIONS

Pulmonary complications remain one of the most common causes of morbidity and mortality. Nimrod Maimon MD, et al [11]., in his review article states that the

lungs are involved in at least 75% of immunocompromised patients with any complication. Mortality rate ranges widely from 15%-90%, depending on the underlying disease, the severity of lung involvement, and the total impairment of host defenses. [11] The development of pulmonary disease in immunosuppressed patients is a diagnostic challenge [11]

Poe RH et al [31]., in his study on Predictors of mortality in the immunocompromised patient with pulmonary infiltrates found a mortality rate of 36%. Rañó A et al[32]., in his study on 200 non-HIV immunocompromised patients found an overall mortality rate of 39%.

These studies show the need for rapid and quick evaluation of pulmonary disease in immunocompromised patients to prevent mortality.

ROLE OF FOB IN DIAGNOSTIC EVALUATION OF PULMONARY INFECTIONS IN NON-HIV IMMUNOCOMPROMISED HOST

Pulmonary diseases in non-HIV immunocompromised patient have a variety of differential diagnosis. Apart from infections different non-infectious causes are also predominant

A Rano et al [8]., in his study on 200 non-HIV immunocompromised patients observed that, in infectious causes when appropriate treatment was changed earlier < 7 days had a better outcome (29% mortality) than treatment changed later (71% mortality). This study highlights the importance that the quick evaluation and treatment modification reduces the mortality

A Similar finding was also observed by DANÉS et al.,[33] in immunocompromised patients where bacterial pneumonia was most common followed by fungal and viral pneumonias. In his study bacterial pneumonia was associated with unilateral and alveolar type of infiltrates. BAL had a diagnostic yield of 52%. Staph aureus was the most common bacterial pathogen and Aspergillus was most common fungal isolates.

FREDERICK W. Kahn et al.,[34] in his study on 94 immunocompromised patients where 100 BAL procedure was done found bronchoscopic yield of 81% for infections. The non-infectious causes observed were malignancy, haemorrhage, pulmonary edema, radiation fibrosis etc. The yield with BAL was similar to that of Trans Bronchial biopsy.

S SHAWGI et al [35]., in a study done on 25 patients with hematological malignancies in INDIA found that overall yield was high with 84%. Bacterial pneumonia alone accounted for 40% and 40% polymicrobial, fungal alone remaining 4%. Pseudomonas was most common bacteria and Aspergillus fumigatus was most common fungi isolated. The therapeutic utility was 24%.

PITFALLLS OF EMPERICAL TREATMENT

More often clinicians treat patients empirically. The mortality may be high if empirical treatment is not modified early once the patient does not improve [8]. It is not possible to cover all diagnostic aetiologies by empirical treatment. Moreover, empiric treatment purely based on clinical criteria alone would be unacceptable given the toxicity associated with such treatment options in most

circumstances. Many of the non-infectious aetiologies are unnecessarily treated with antimicrobials contributing to drug resistance and toxicity. Also, most non-infectious causes are also potentially fatal if not diagnosed and treated correctly. Finally, many non-infectious conditions like DAH may require corticosteroids for their management, which may exacerbate the underlying pulmonary infections if not ruled out properly. Hence ruling out infections thoroughly is mandatory before starting corticosteroid therapy for management of non-infectious causes and also for continuing immunosuppresive therapy [11].

Infections in immunocompromised hosts often present without the expected signs and symptoms of infection. Many non-infectious cause like DAH, radiation pneumonitis, malignancy may also present with fever mimicking infections. Hence clinicians must follow an aggressive approach and must have a low threshold for performing investigations when encountered with an immunocompromised patient with pulmonary diseases. Invasive studies such as bronchoscopy or biopsy are best performed early in the course of possible infection and prior to the initiation of antimicrobial therapy [36].

DRAWBACKS OF NON-INVASIVE TECHNIQUES

The non-invasive diagnostic methods include serologic tests, blood antigen detection, nasopharyngeal wash, sputum, and tracheobronchial aspirate cultures, chest radiograph, CT chest, sputum AFB staining, Grams staining, Skin tests etc. Though blood cultures are done routinely, they have a low diagnostic yield.

A Rano et al [8]., in his study found that yield of blood culture was only 16% & sputum culture with 30%. Bronchoscopic yield was 59%. Thus he concluded that BAL had a higher diagnostic yield and impact on therapeutic decisions. Also Sputum culture is valuable only when the organisms not routinely found in oropharyngeal secretions are isolated like mycobacteria, Mycoplasma etc [11].

Danes et al [33]., in his study found that non-invasive technique like sputum culture was associated with low yield of only 20%, blood culture with 8%, and nasopharyngeal wash for viral antigen detection was only 6%, compared to bronchoscopic yield of around 66%.

Though standard chest radiograph can be used as a screening tool in immunocompromised patients with chest symptoms, studies have advocated early use of CT scans. A study in renal transplant recipients showed that though chest radiograph was initially normal in patients with pulmonary complaints subsequent CT scan demonstrated abnormalities [37]. Heussel et al [38]., in a study on 87 patients with febrile neutropenia found that in 50% patients CT revealed lesions that were not visualized by chest radiography. Thin section CT was able to detect pneumonia 5 days earlier compared to chest radiograph. CT in addition to identifying lesion missed on chest radiography helps to guide invasive diagnostic procedures like BAL, TBLB etc.

Even though the non-invasive diagnostic techniques are safe and relatively low cost studies have shown that they add little useful information [8,11,39]. The overall diagnostic yield of non-invasive techniques ranges from 10%-30% [8,33].

Hence, due to varied aetiology of pulmonary diseases along with non-specific nature of clinical and radiological presentation coupled with low yields of non-invasive techniques makes invasive diagnostic procedures mandatory. The benefit to risk ratio is an important consideration when choosing an invasive procedure in immunocompromised patients who are already critically ill due to the underlying disease. The invasive procedure with good yield and low risk in most of the studies is BAL.[11,40,41] Lavage is safe, minimally invasive, reproducible and leads to a quick diagnosis. Suitable even for very sick and critically ill patients with less complications. The yield of BAL is better than of Protected brush Sampling, although PBS is more specific.[42,43]

Jennifer A Crockett, MD et al [42]., in his study found that yield of BAL was 38% compared to PBS with 10% and TBB with 27%. Adding BAL, PBS, Transbronchial biopsy during the bronchoscopic procedure increases the diagnostic yield, sensitivity and specificity at the same time complication rate of the procedure [43].

Rano et al [8], in his study found that BAL had the best diagnostic yield of 51%, better than PBS (24%), with only 3 minor complications and led to treatment modification in 38%.

Gruson D et al [44]., studied the role of bronchoscopy in the management of pulmonary infiltrates in neutropenic patients found that BAL had a complication rate of 17% and acceptable yield of 49%

AIMS AND OBJECTIVES

PRIMARY OBJECTICTIVES

- To study the

  DIAGNOSTIC YIELD OF BRONCHOSCOPY

  MODIFICATION OF CURRENT EMPIRICAL TREATMENT AS THE RESULT OF BRONCHOSCOPIC INTERVENTION.

among NON-HIV immunocompromised patients presenting with pulmonary diseases in a tertiary care center.

SECONDARY OBJECTIVES:

- To collect data on etiology of different microorganisms among Non-HIV immunocompromised patients.
- To collect data on non-infectious causes of pulmonary diseases in Non-HIV immunocompromised patients in our tertiary care center.
- Compare symptoms at the time of presentation, with bronchoscopic yield.
- Compare the different radiological pattern, with bronchoscopic yield.
- Compare different subgroups of Non-HIV immunocompromised patients with regards to presenting symptoms, radiological patterns, bronchoscopic yield, treatment modification, different spectrum of infections & complications.

MATERIALS & METHODS

STUDY CENTER

The study was conducted in Rajiv Gandhi Government General Hospital, Park Town, Chennai, which is a tertiary care institute**.**

STUDY DESIGN:

- The study was a prospective observational study.
- Consecutive immunocompromised patients who presented with pulmonary diseases were included in the study.
- No specific method of randomization was used.
- No controls were used in the study.

STUDY PERIOD:

8 months, from January 2016 – August 2016.

SUBJECT SELECTION:

A total 592 patients referred from other departments like Oncology, Nephrology, Rheumatology, Hematology from January 2016 – July 2016 above the age of 12 years to Thoracic medicine department for evaluation of pulmonary diseases were screened.

INCLUSION CRITERIA:

Among them 120 patients satisfying definition of immunosuppression with any one of the following features were evaluated,

1. Chest symptoms like cough, sputum, breathlessness, chestpain, hemoptysis with or without fever.
2. Abnormal auscultatory finding like crackles, wheeze with or without symptoms.
3. Presence of pulmonary infiltrates in radiography

Immunosuppression was defined by standard guidelines using IDSA [9] and CDC [4] guidelines on vaccination for immune compromised host.

DEFINITION FOR IMMUNOSUPPRESSION

1. Receiving cancer chemotherapy
2. Receiving daily corticosteroid therapy with a dose ≥20 mg of prednisone or equivalent for ≥14 days
3. Receiving certain biologic immune modulators, that is, tumor necrosis factor-alpha (TNF-α) blocker or rituximab
4. Those receiving methotrexate (MTX) ≤0. 4 mg/kg/week, azathioprine ≤3 mg/kg/day, or 6-mercaptopurine ≤1. 5 mg/kg/day
5. Solid organ transplant recipients
6. Hematological malignancies
7. Chronic kidney disease on hemodialysis

EXCLUSION CRITERIA:

Out of the 120 patients satisfying inclusion criteria 30 patients were excluded from the study based on the following reasons,

1. All HIV positive patients were excluded from the study.
2. All sputum AFB smear positive pulmonary tuberculosis were excluded from the study.
3. Patients having very poor general condition, very severe breathlessness, recent history of myocardial infarction and patients not fit for bronchoscopy.
4. Patients not willing to give informed written consent.

METHODOLOGY

- Bronchoscopy was planned in the remaining 90 patients and they underwent complete clinical evaluation.

Informed consent was obtained after explaining the nature of the study.

1. The following data were collected from the patient
    - Name, Age, Sex, Residential address, Occupation
2. Detailed clinical history was collected which included
    - The presenting complaints/symptoms and their duration, including presenting illness.
    - The nature of the primary disease for which patients are undergoing current treatment like, Chronic Kidney Disease, Rheumatological Diseases, Carcinoma, Hematological diseases etc.

- The past history of any similar illness or respiratory problems
- A detailed treatment history, which includes the immunosuppressive agents patients are currently receiving like corticosteroids, Biological Agents, chemotherapeutic agents etc., their dosage and duration.
- Personal history, family history and occupational history
- History of any comorbidities such as coronary artery disease, recent MI, systemic hypertension, Diabetes Mellitus etc.

3. General examination and a structured clinical examination of the respiratory system and other systems were done.
4. Basic blood investigations were done in all patients like Complete blood count, Renal function test, Bleeding time, Clotting time, Prothrombin time, Activated partial thromboplastin time.
5. Chest Skiagram anteroposterior, lateral view, routinely Plain computed tomography (CT CHEST) chest/contrast enhanced computed tomography chest (CECT-CHEST)/ High resolution computed tomography chest (HRCT-CHEST) were done as required depending on the patient's diagnosis and clinical status.
6. A careful pre-evaluation and cardiac fitness which includes an echo was done prior to Fiber optic bronchoscopy (FOB) in all patients.

➢ After complete clinical evaluation, blood investigations and pre procedure evaluation ,10 patients were excluded from the study for following reasons

- Very high cardiac risk
- Coagulation abnormalities or very low platelet count < 50,000 cells/mm3

- The remaining 80 patients included in study were already receiving empirical antimicrobial therapy for their abnormal symptoms, signs or radiological lesions by the treating physician. Out of which 11 patients who showed clinical improvement to the current empirical treatment as noted by the treating physician during pre-procedure evaluation were further excluded from the study.
- The remaining 69 underwent bronchoscope. Bronchoscopy (FOB) was done as per British Thoracic Society guideline for diagnostic flexible bronchoscopy in adults using an Olympus fiber optic bronchoscope and strict disinfection protocol was followed for disinfecting the scope pre and post bronchoscopy as per the above mentioned guidelines [45]
- In 4 patients bronchoscopy could not be completed due to poor patient cooperation were further excluded from the study

SAMPLE SIZE

A total 65 patients FOB was completed and BAL sample was sent for analysis

ANALYSIS OF BAL SAMPLE

Bronchoalveolar lavage was done from the lobe affected and segment involved and sample collected was sent for

- GENE XPERT MTB [46] – A real time cartridge based nucleic acid amplification test for diagnosis of Mycobacterium Tuberculosis done at STATE INTERMEDIATE LEVEL REFERENCE

LABORATORY AND INSTITUTE OF THORACIC MEDICINE, CHETPET.

- AFB staining
- Bacterial culture and sensitivity & Grams staining
- Fungal culture & KOH staining
- Cytology

During bronchoscopy

- Transbronchial & Endobronchial biopsy was done as required on case to case basis provided there were no contraindications to procedure like, prolonged bleeding time, clotting time, severe hypoxemia likely to worsen during bronchoscopy, Poor general condition, unstable cardiovascular status, advanced renal failure etc [47,48].

TECHNIQUE OF BRONCHOALVEOLAR LAVAGE [49]

- Bronchoalveolar Lavage was done as per the standard guidelines prescribed by European Respiratory Task Force – Recommendation of standardized of BAL Technique (1999) [49]

PROCESSING OF BRONCHO ALVEOLAR LAVAGE SAMPLE

The BAL sample obtained was collected in a sterile container (sterile uricol). They were then transported as early as possible to the lab in sample carrier with ice packs. If any delay in transport they were stored immediately in the refrigerator at (2-8˚C).

SAMPLE PROCESSING [50]

The samples were immediately processed after reaching the lab using standard microbiological techniques. Routine methods like Gram's staining and AFB (Acid Fast Bacilli) staining were done on all samples. Then they were inoculated on standard culture media for detecting bacterial growth like blood agar and Mac Conkey agar (MAC). Culture for fungi was done by using Sabouraud's Dextrose Agar (SDA) medium. To check the presence of fastidious organisms and also to rule out the presence of anaerobic organisms special media like Thioglycollate broth (TGB) was also inoculated.

The plates and tubes were incubated at 37C in an incubator. The blood agar plates were incubated in a candle jar with 5-10% Co2. After overnight incubation, the plates and tubes were examined for presence of growth. The TGB tubes were incubated till 7 days before declaring a negative result. The SDA plates were incubated for 4 weeks to allow for the growth of slow growing fungi.

If growth was present in Blood agar (BA) and MAC plates, then the significance of the growth was assessed by doing a colony count. In a BA plate the hemolysis produced by the colonies are noted. Standardized tests like catalase and oxidase tests were performed on colonies from non-selective medium.

Identification of the bacterial species is done by using standard biochemical tests like an Indole test (using Kovac's reagent), MMM medium (Mannitol Motility Medium), citrate test, urease test, Triple Sugar Iron medium (TSI) and sugar fermentation tests.

Identification of the fungal species is done by detecting growth in SDA plates and doing an LPCB (Lacto Phenol Cotton Blue) mount on the culture. Yeasts like Candida were identified using Gram's staining, germ tube test and assimilation and fermentation tests. Speciation of Candida was done using a special media called CHROM agar.

DIAGNOSTIC CRITERIA TO DETERMINE INFECTIOUS ETIOLOGY IN BAL

1. **TUBERCULOSIS:** AFB staining positive in lavage fluid or MTB detected by CBNAAT (Real Time Cartridge Based Nucleic Acid Amplification Method)
2. **BACERIAL INFECTIONS:** BAL fluid contains >=10^4 CFU/ml in cultures of BAL 1 ml and < 1% squamous epithelial cells in Geimsa stained smears[51,34]
3. **FUNGAL INFECTIONS**: (**E**uropean **O**rganization for **R**esearch and **T**reatment of **C**ancer/Invasive Fungal Infections Cooperative Group DEFINITION WAS USED)

- Revised Definitions of Invasive Fungal Disease from the **E**uropean **O**rganization for **R**esearch and **T**reatment of Cancer/Invasive Fungal Infections **C**ooperative Group and the National Institute of Allergy and Infectious Diseases Mycoses Study Group (EORTC/MSG) Consensus Group[52]

- **Criteria for proven invasive fungal disease except for endemic Mycoses**

❖ **Microbiological analysis:**

Histopathologic, cytological or direct microscopic examination of a specimen obtained by needle aspiration or biopsy in which hyphae or melanized yeast-like forms are seen accompanied by evidence of associated tissue damage

❖ **Culture**

Recovery of a mold or "black yeast" by culture of a specimen obtained by a sterile procedure from a normally sterile and clinically or radiologically abnormal site consistent with an infectious disease process, excluding bronchoalveolar lavage fluid, a cranial sinus cavity specimen, and urine

- **Criteria for probable invasive fungal disease except for Endemic Mycoses**

1. **Host factors:**
    a. Recent history of neutropenia (<500 neutrophils/mm^3 for >10 days) temporally related to the onset of fungal disease
    b. Receipt of an allogeneic stem cell transplant
    c. Prolonged use of corticosteroids (excluding among patients with allergic bronchopulmonary aspergillosis) at a mean minimum dose of 0.3 mg/kg/day of prednisone equivalent for >3 weeks
    d. Treatment with other recognized T cell immunosuppressants, such as cyclosporine, TNF-α blockers, specific monoclonal

antibodies (such as alemtuzumab), or nucleoside analogues during the past 90 days

e. Inherited severe immunodeficiency (such as chronic granulomatous disease or severe combined immunodeficiency)

2. **Clinical criteria: Lower respiratory tract fungal disease**

The presence of 1 of the following 3 signs on CT:

a. Dense, well-circumscribed lesions(s) with or without a halo sign

b. Air-crescent sign

c. Cavity

3. **Mycological criteria:**

A. DIRECT TEST (cytology, direct microscopy, or culture)

Mold in sputum, bronchoalveolar lavage fluid, bronchial brush, or sinus aspirate samples, indicated by 1 of the following:

- Presence of fungal elements indicating a mold
- Recovery by culture of a mold (e.g., Aspergillus, Fusarium, Zygomycetes, or Scedosporium species)

B. INDIRECT TESTS (detection of antigen or cell-wall constituents)

Aspergillosis

- Galactomannan antigen detected in plasma, serum, BAL fluid, or CSF
- Invasive fungal disease other than cryptococcosis and zygomycoses
- β-d-glucan detected in serum

CRITERIA FOR THE DIAGNOSIS OF ENDEMIC MYCOSES

(Endemic Mycoses includes histoplasmosis, blastomycosis, coccidioidomycosis, paracoccidioidomycosis, sporotrichosis, and infection due to Penicillium marneffei.)

PROVEN ENDEMIC MYCOSIS

In a host with an illness consistent with an endemic mycosis, 1 of the following:

a. Recovery in culture from a specimen obtained from the affected site or from blood
b. Histopathologic or direct microscopic demonstration of appropriate morphological forms with a truly distinctive appearance characteristic of dimorphic fungi, such as Coccidioides species spherules, Blastomyces dermatitidis thick-walled broad-based budding yeasts, Paracoccidioides brasiliensis multiple budding yeast cells, and, in the case of histoplasmosis, the presence of characteristic intracellular yeast forms in a phagocyte in a peripheral blood smear or in tissue macrophages

PROBABLE ENDEMIC MYCOSIS

The presence of a host factor, including but not limited to those specified plus a clinical picture consistent with endemic mycosis and Mycological evidence, such as a positive Histoplasma antigen test result from urine, blood, or CSF

TREATMENT MODIFICATION & FOLLOW UP

- Patients were allowed to continue with same empirical treatment until the results of bronchoscopy were available.
- Appropriate Treatment modification was done based on the results.
- Patients diagnosed as tuberculosis were started on Anti-Tuberculous Treatment.
- For bacterial infections antimicrobials were changed as per culture sensitivity pattern if needed.
- For fungal infections antifungals were started in patients with proven and probable invasive fungal infections.
- Patients diagnosed with malignancy and lymphoma were referred back to oncology department for restarting chemotherapeutic regimens.

Patients were followed up until the signs of clinical improvement or discharge or death in hospital. Post discharge patients were enquired for clinical improvement during their follow up visits to the hospital or through telephone calls.

DEFINITIONS

INFECTIOUS ETIOLOGY

When microorganisms grown in culture consistent with above diagnostic criteria for bacterial or fungal infections or BAL fluid AFB smear positive or MTB detected in GeneXpert.

NON-INFECTIOUS ETIOLOGY

No organism isolated from a bacterial/fungal culture or AFB staining negative or GeneXpert MTB not detected.

PLUS

Alternative diagnosis established by cytology positive for malignant cells or HPE proof for lymphomatous infiltration or malignancy or radiation fibrosis or DAH was diagnosed by established criteria [53,54]

POSITIVE YEILD OF FOB:

When an infectious or non-infectious cause was established by bronchoscopy.

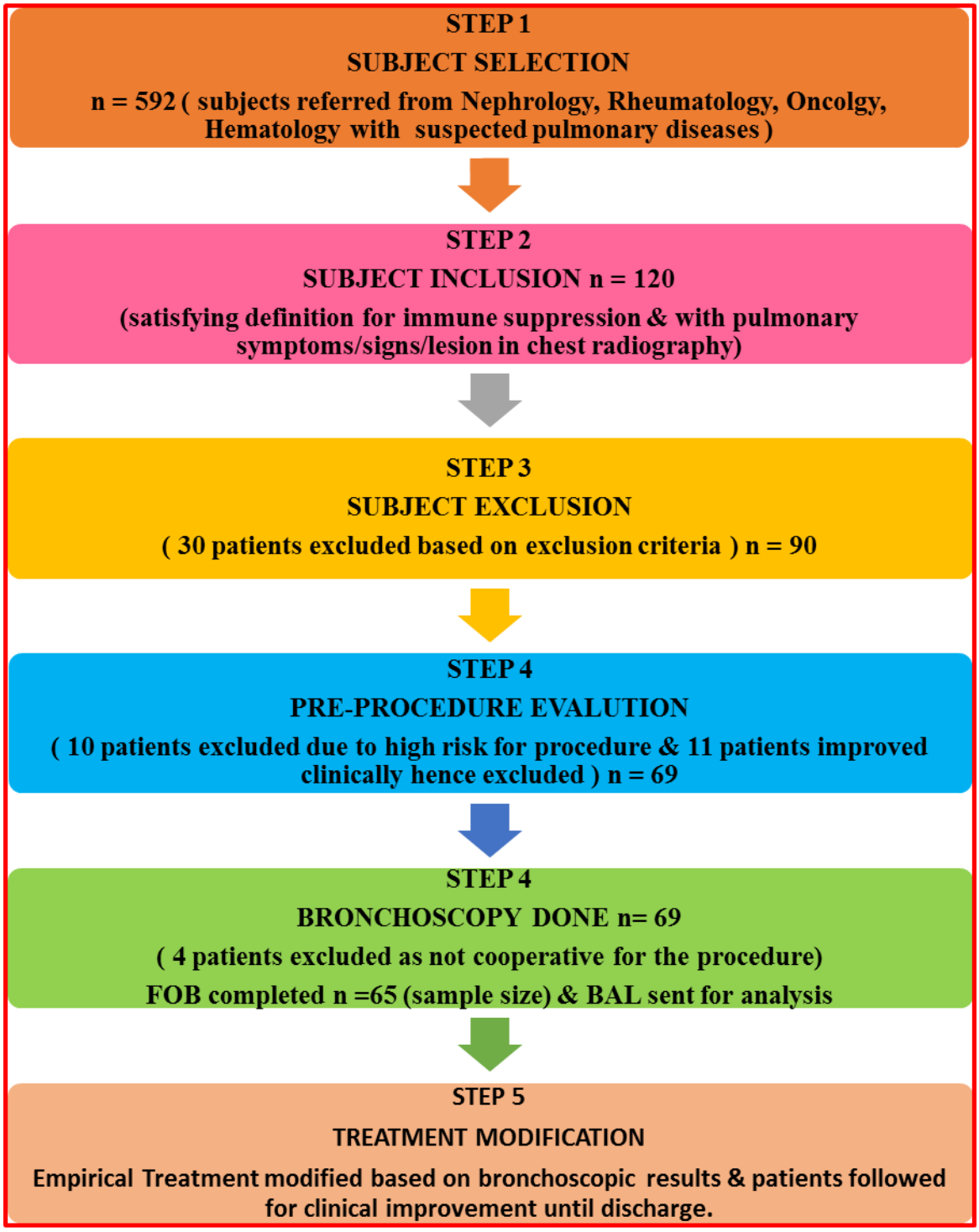
NEGATIVE / NON-DIAGNOSTIC YEILD:

When no definitive infectious or non-infectious cause could be established by bronchoscopy.

STATISTICAL ANALYSIS:

All statistical analysis was performed using the Statistical Package for Social Science (SPSS, version 17) for Microsoft windows. Descriptive statistics were presented as numbers and percentages A chi-square test was used for comparison between two attributes. A two-sided p value < 0.05 was considered statistically significant.

STUDY PROTOCOL



RESULTS AND ANALYSIS

AGE DISTRIBUTION:

A total number of 65 patients were included in the study.

The mean age of 65 patients was 41.91 with a standard deviation of 15.5. The age of patients ranged from 15 years – 74 years. The patients were equally divided among two age groups < 40 years & > 40 years with 51% and 49% respectively.

TABLE 3: AGE DISTRIBUTION

AGE DISTRIBUTION 41.91 +/- 15.5		
	Freq	**Percentage**
< 40 YEARS	33	51%
> 40 YEARS	32	49%
TOTAL	**65**	**100**

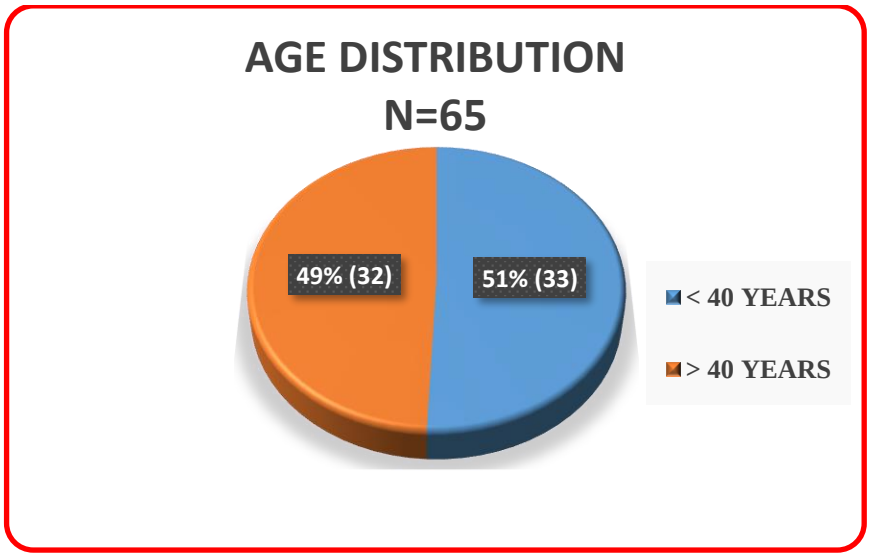


FIG 1: AGE DISTRIBUTION

GENDER DISTRIBUTION:

Out of 65 patients included in study 36 were male and 29 were females. Thus, ratio was 55% & 45% male to female.

TABLE 4: GENDER DISTRIBUTION

GENDER DISTRIBUTION		
	FREQ	**%**
MALE	36	55%
FEMALE	29	45%
TOTAL	**65**	**100%**

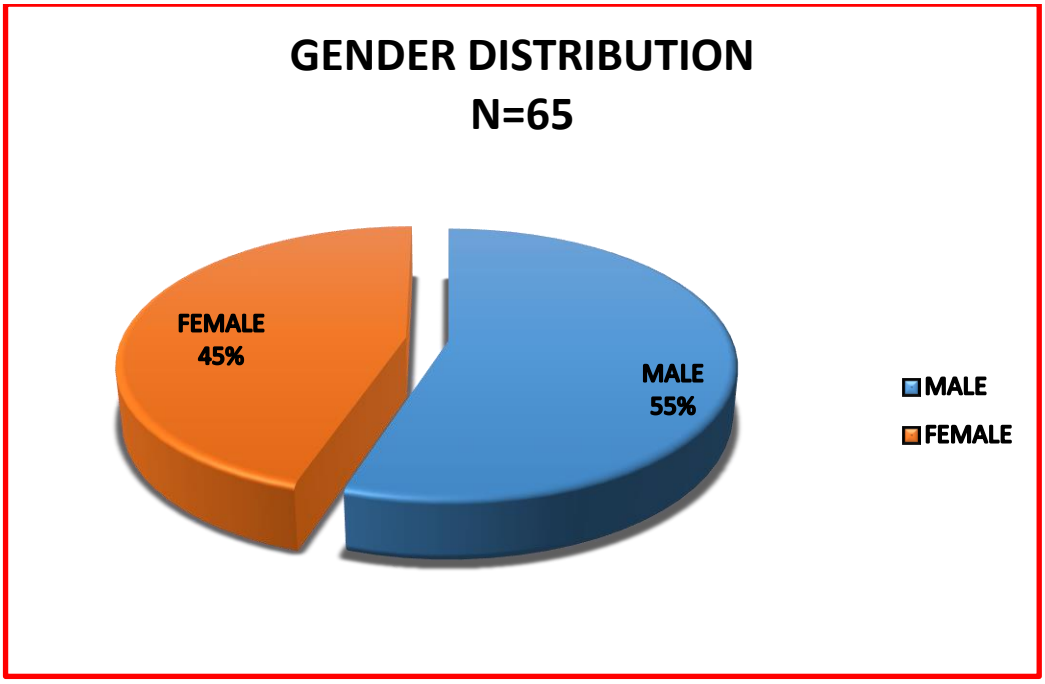


FIG 2: GENDER DISTRIBUTION

DIFFERENT GROUP OF IMMUNOCOMPROMISED PATIENTS INCLUDED IN THE STUDY

The 65 patients included in the study were divided into 5 groups based on their disease pattern and nature of immunosuppresion

GROUP 1: Cancer patients who were receiving chemotherapy in past 6 months

GROUP 2: Post Renal Transplant recipients who were receiving immunosuppresants.

GROUP 3: Chronic Renal Failure patients currently receiving haemodialysis

GROUP 4: Patients with Hematological Malignancies who were immunosuppressed because of their disease per se as well as receiving chemotherapy

GROUP 5: Connective Tissue Disease patients like SLE, RA, etc, who were receiving steroids > 20 mg/day for more than 1 month or receiving immunosuppressive drugs or Biological agents.

TABLE 5: DIFFERENT GROUPS OF IMMUNOCOMPROMISED PATIENTS

DIFFERENT GROUPS OF IMMUNOCOMPROMISED PATIENTS		
	FREQ	**PERCENTAGE**
CANCER CHEMOTHERAPY GROUP	11	17%
POST RENAL TRANSPLANT GROUP	9	14%
CHRONIC KIDNEY DISEASE GROUP	16	25%
HAEMATOLOGICAL MALIGNANCIES	8	12%
CONNECTIVE TISSUE DISEASES	21	32%
TOTAL	**65**	**100%**

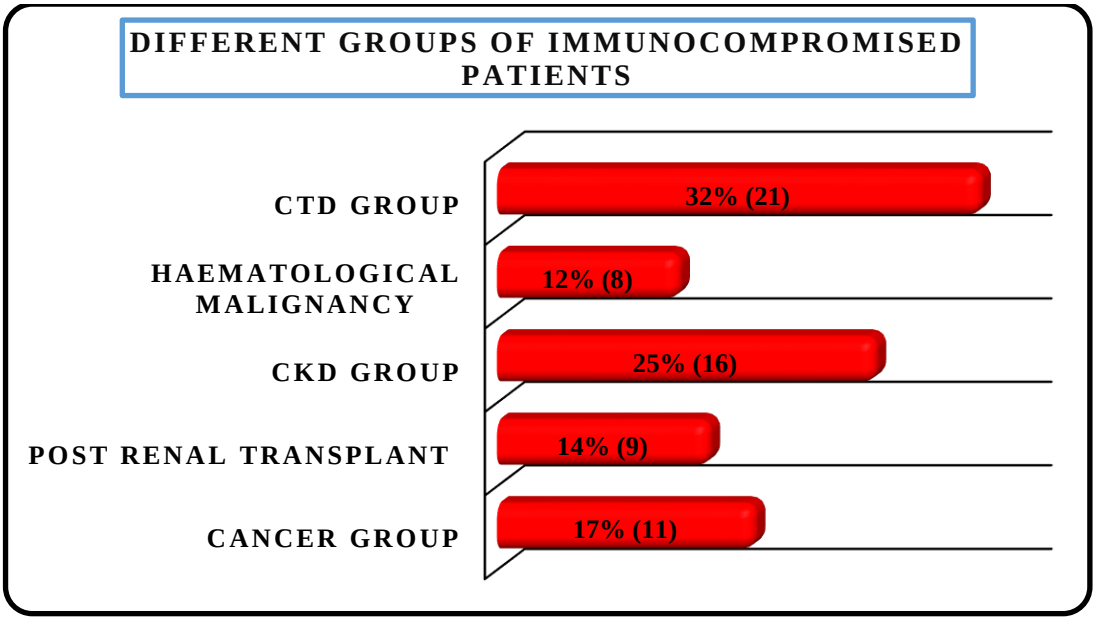


FIG 3: DIFFERENENT GROUPS OF IMMUNOCOMPROMISED PATIENTS

PRESENTING SYMPTOMS

The presenting symptoms of the patients were

- **CHEST SYMPTOMS ALONE**: Consisted of cough with expectoration, dry cough, Dyspnea, Chest pain etc.
- **CHEST SYMPTOMS ALONG WITH FEVER**
- **FEVER ALONE**
- **HEMOPTYSIS**
- **ASYMPTOMATIC**

TABLE 6: PRESENTING SYMPTOMS

PRESENTING SYMPTOMS		
	FREQ	**%**
CHEST SYMPTOMS ALONE	36	55%
CHEST SYMPTOMS WITH FEVER	11	17%
HEMOPTYSIS	9	14%
FEVER ALONE	6	9%
ASYMPTOMATIC	3	5%
TOTAL	**65**	**100%**

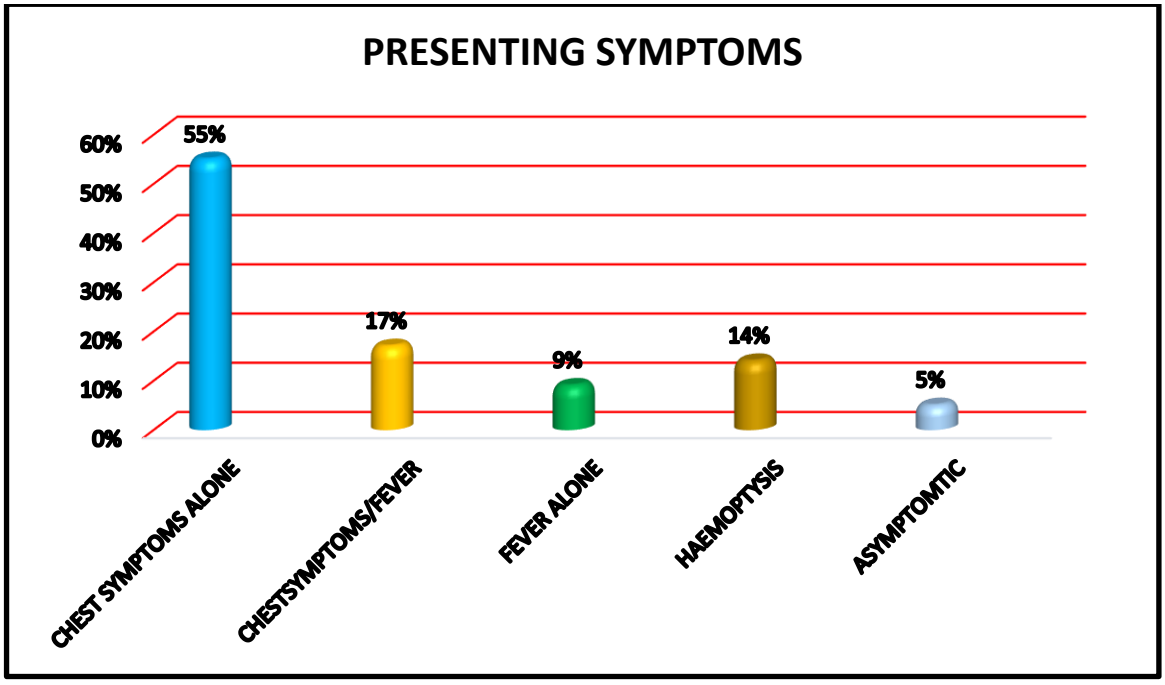


FIG 4: PRESENTING SYMPTOMS

DURATION OF SYMPTOMS

Duration of symptoms was divided into 4 groups:

- ACUTE ONSET - < 3 weeks
- SUBACUTE ONSET – 3-8 weeks
- CHRONIC - > 8 weeks
- ASYMPTOMATIC

TABLE 7: DURATION OF SYMPTOMS

DURATION OF SYMPTOMS		
	FREQ	**%**
< 3 WEEKS	34	52%
3-8 WEEKS	20	31%
> 8 WEEKS	8	12%
ASYMPTOMATIC	3	5%
TOTAL	**65**	**100%**

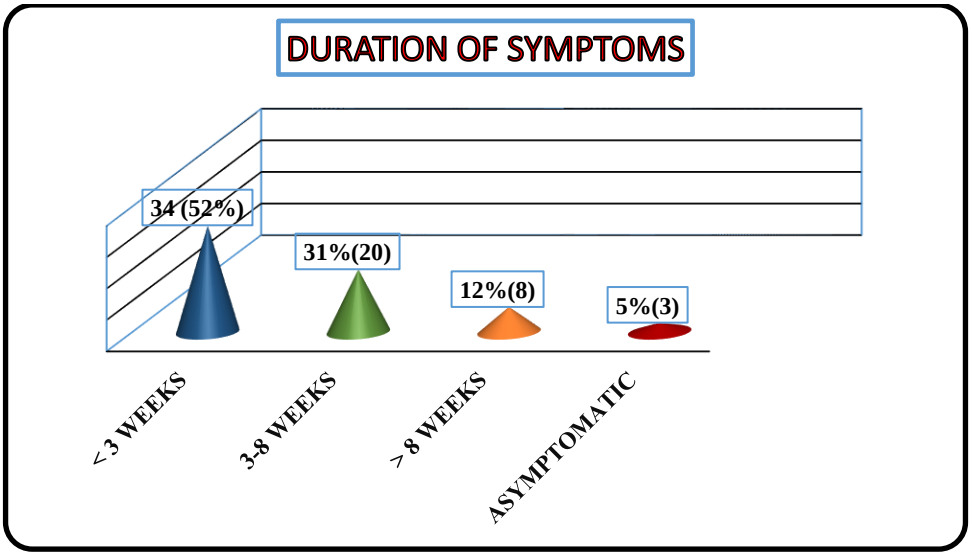


FIG 5: DURATION OF SYMPTOMS

RADIOLOGICAL FINDINGS

The radiological findings at the time of presentation were divided into followings groups based on the predominant pattern as assessed by the pulmonologist

- Consolidation pattern, Ground Glass Opacities, Tree-in-Bud pattern, Cavity, Reticular & Nodular pattern.

TABLE 8: RADIOLOGY

DIFFERENT FORMS OF RADIOLOGICAL INVOLVEMENT		
	FREQ	**%**
CONSOLIDATION	31	48%
GROUND GLASS OPACITIES	9	14%
CAVITY	7	11%
TREE IN BUD APPEARANCE	4	6%
RETICULAR PATTERN	8	12%
NODULAR PATTERN	6	9%
TOTAL	**65**	**100%**

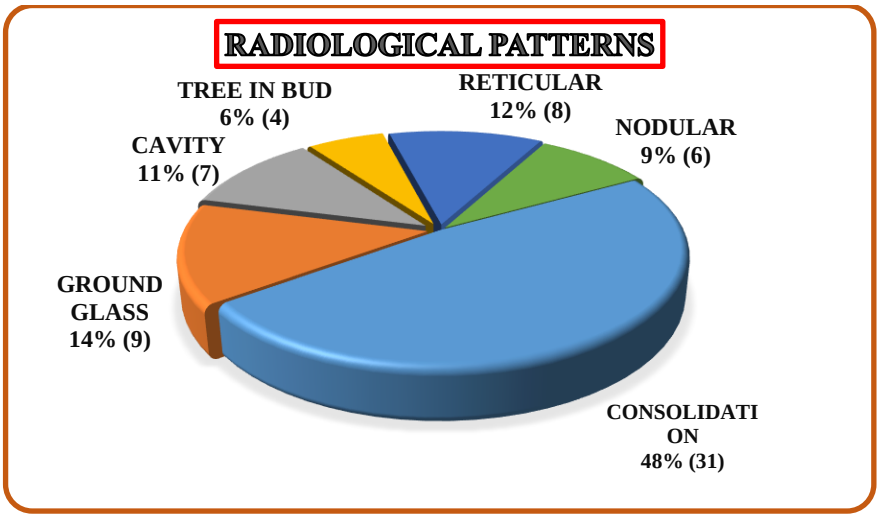


FIG 6: DIFFERENT PATTERNS OF RADIOLOGICAL INVOLVEMENT

ALVEOLAR VS NON-ALEOLAR PATTERN

Consolidation, GGO, Cavity, Tree in Bud were considered together as alveolar pattern and Reticular & Nodular predominant forms were considered as non-alveolar pattern

TABLE 9: ALVEOLAR VS NON-ALVEOLAR PATTERN

ALVEOLAR VS NON-ALVEOLAR PATTERN		
	FREQ	%
ALVEOLAR PATTERN	51	79%
NON-ALVEOLAR PATTERN	14	21%
TOTAL	**65**	**100%**

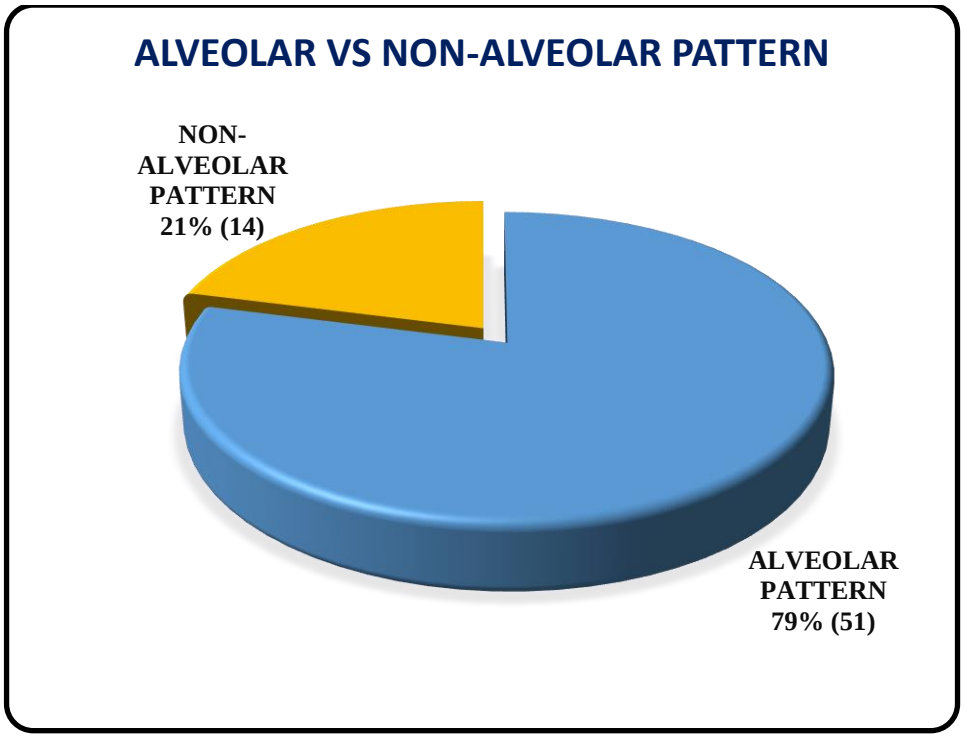


FIG 7: ALVEOLAR VS NON-ALVEOLAR PATTERN

LOBE INVOLVEMENT (CT CHEST)

In our study lobe involvement was divided into Upper Lobe, Middle Lobe/ Lingula, Lower Lobe.

TABLE: 10: LOBE INVOLVEMENT IN CT-CHEST

LOBE INVOLVEMENT		
LOBE	**FREQ**	**%**
UPPER LOBE	21	32%
MIDDLE LOBE/ LINGULA	17	26%
LOWER LOBE	27	41%
TOTAL	**65**	**100%**

FOCAL VS DIFFUSE INVOLVEMENT

Involvement of single lobe was considered as focal & involvement of 2 or more lobes was considered as diffuse.

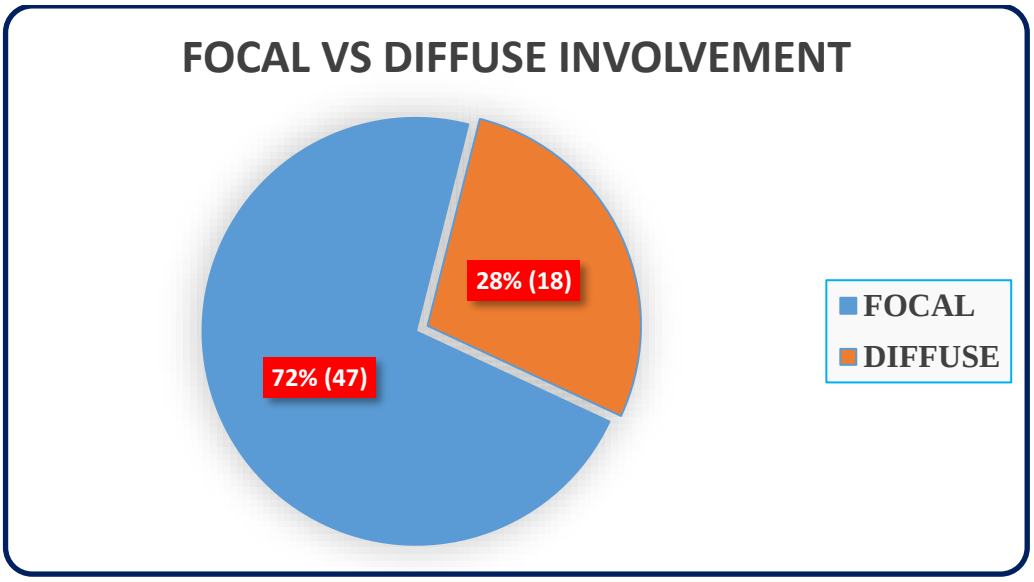


FIG 8: FOCAL VS DIFFUSE INVOLVEMENT OF LOBES

YIELD OF BRONCHOSCOPY

In our study bronchoscopy gave positive results in 80% (52 cases) and no diagnosis could be obtained even after bronchoscopy in 20% (13 cases)

POSITIVE YIELD: Yield considered to be positive when infectious etiology like TB (diagnosed by Bronchial Wash GeneXpert/ AFB smear positivity), BACTERIAL, FUNGAL organisms were diagnosed by culture OR noninfectious causes were diagnosed by Histopathological examination & cytology.

NEGATIVE YIELD: when no diagnosis could be obtained.

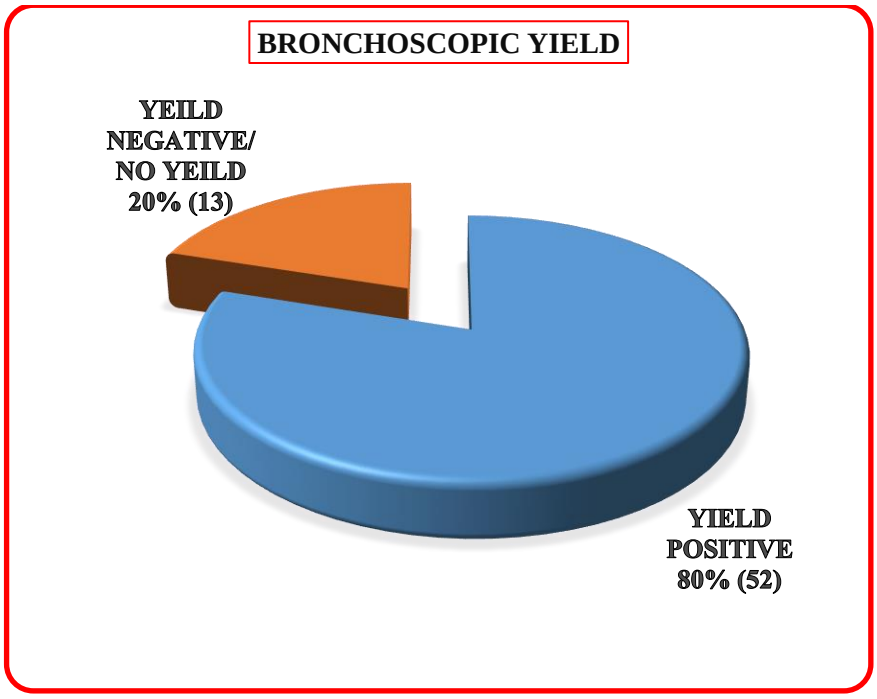


FIG 9: YIELD OF BRONCHOSCOPY

INFECTIOUS VS NON-INFECTIOUS ETIOLOGY DIAGNOSED BY BRONCHOSCOPY

Out of the 80 % (52 cases) of positive bronchoscopic yield 65% (42) were due to infectious etiology and remaining 15% (10) were due to non-infectious causes.

TABLE 11: YIELD OF BRONCHOSCOPY

BRONCHOSCOPIC YEILD	FREQ	%
INFECTOIUS ETIOLOGY	42	65%
NON-INFECTIOUS ETIOLOGY	10	15%
NO DIAGNOSIS OBTAINED	13	20%
TOTAL	65	100%

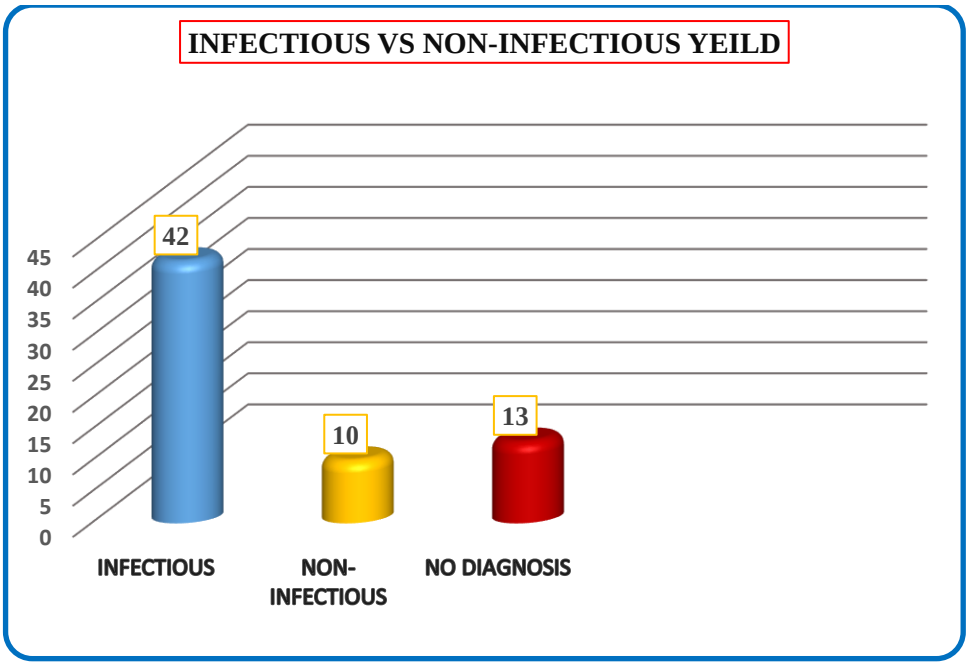


FIG 10: INFECTIOUS VS NON-INFECTIOUS ETIOLOGY – BY BRONCHOSCOPY

SPECTRUM OF PULMONARY INFECTIONS

Among the infectious causes of pulmonary diseases in immunocompromised patients Bacterial infections were predominant with 24%, followed by mixed infections by 15%, tuberculosis 14% & fungal 12%

TABLE 12: SPECTRUM OF PULMONARY INFECTIONS

ORGANISM IDENTIFIED		
	FREQ	**%**
BACTERIAL ALONE	15	24%
TUBERCULOSIS ALONE	9	14%
FUNGAL ALONE	8	12%
MIXED	10	15%
NON-INFECTIOUS	10	15%
NO DIAGNOSIS	13	20%
TOTAL	**65**	**100%**

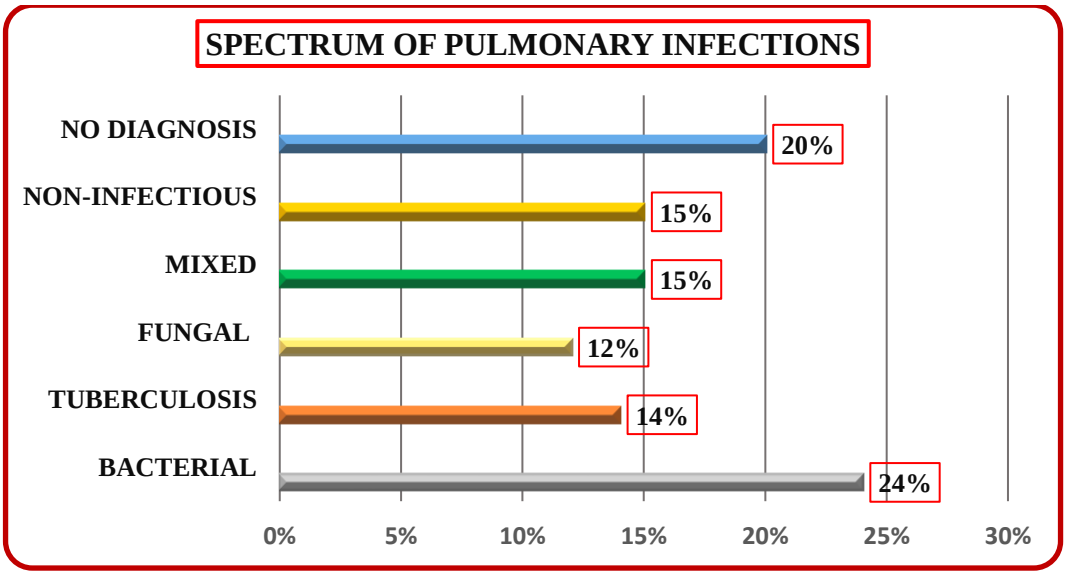


FIG 11: SPECTRUM OF PULMONARY INFECTIONS

TYPES OF MIXED ORGANISMS IDENTIFIED

TABLE 13: PATTERN OF MIXED ORGANISMS

ORGANISMS	FREQ
TUBERCULOSIS + BACTERIAL	3
TUBERCULOSIS + FUNGAL	2
BACTERIAL + FUNGAL	4
TUBERCULOSIS + BACTERIAL+ FUNGAL	1
TOTAL	**10**

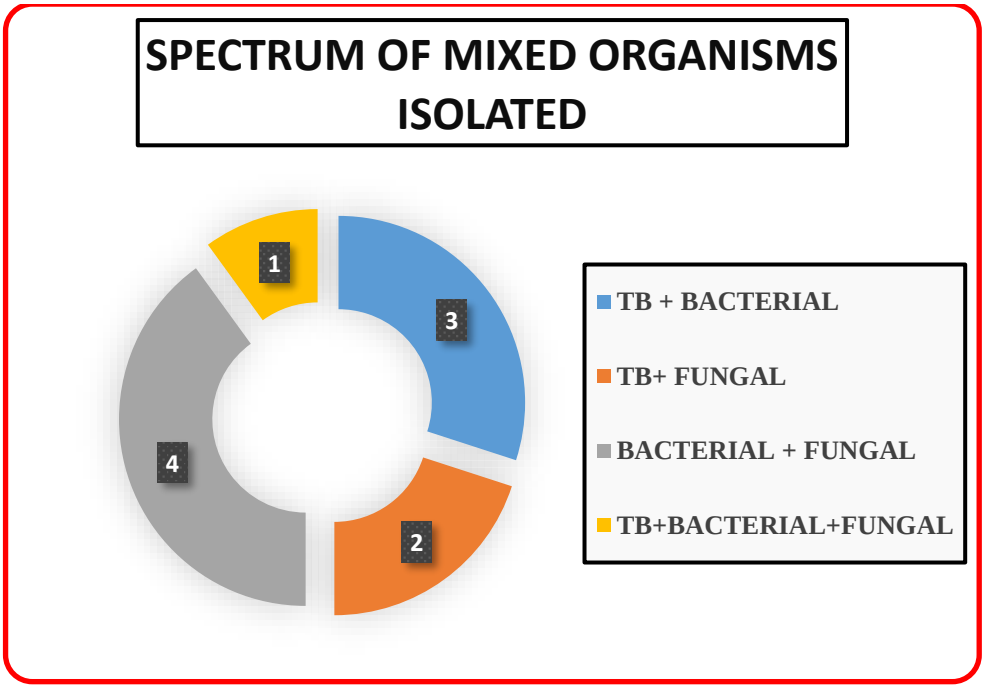


FIG 12: SPECTRUM OF MIXED ISOLATES

SPECTRUM OF BACTERIAL INFECTIONS

Overall out of 65 patients in the study bronchial wash bacterial culture was positive in 22 patients. In one patient two organisms were isolated. So totally 23 organisms isolated contributing to 35% of infection in immunocompromised patients.

TABLE 14: SPECTRUM OF BACTERIAL INFECTIONS

BACTERIAL ISOLATES IDENTIFIED BY BAL CULTURE		
	FREQ	**%**
BACTERIAL ALONE	15	23%
BACTERIAL + OTHER ORGANISMS (TB/ FUNGAL)	8	12%
NEGATIVE FOR BACTERIAL CULTURE	42	65%
TOTAL	**65**	**100%**

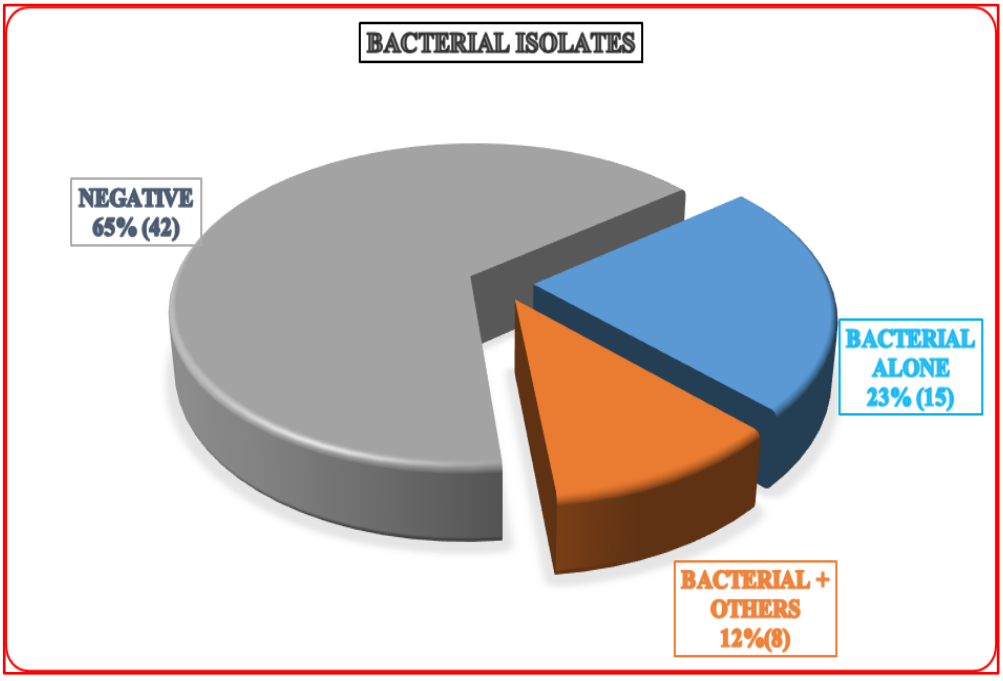


FIG 13: PROPOTION OF BACTERIAL INFECTIONS DIAGNOSED BY BAL CULTURE

BAL BACTERIAL CULTURE RESULTS

TABLE 15: BACTERIA ISOLATED FROM CULTURE

BACTERIA ISOLATED		
	FREQ	**%**
STREPTOCOCCUS PNEUMONIAE	1	1.5%
KLEBSIELLA PNEUMONIAE	5	7.5%
PSEUDOMONAS AERUGINOSA	7	10.5%
ACINETOBACTER	3	4.5%
MRSA	5	7.5%
ENTEROCOCCI	2	3%
E. COLI	1	1.5%

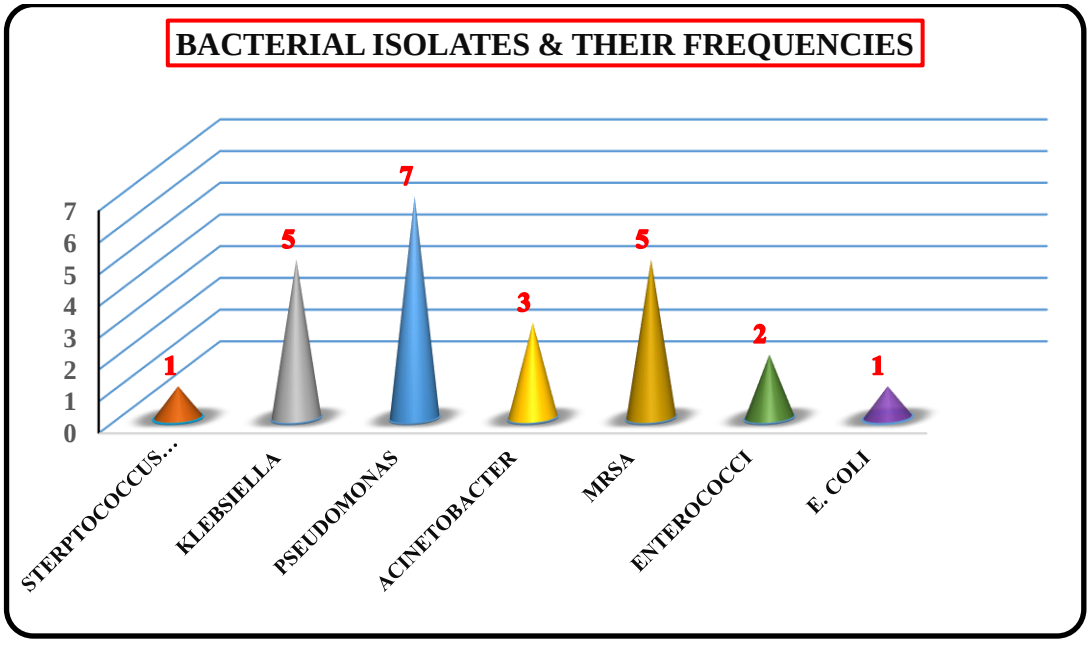


FIG 14: SPECTRUM OF BACTERIAL INFECTIONS

SPECTRUM OF FUNGAL INFECTIONS

Out of 65 patients in whom BAL was done fungal culture was positive in 15 cases, contributing to 23% of pulmonary infections. Out of 15 BAL fungal culture positive, in 8 patients, fungi were alone, isolated & in remaining 7 cases, fungi were isolated with other organisms (Bacterial/TB)

TABLE 16: SPECTRUM OF FUNGAL INFECTIONS

FUNGAL ORGANISMS ISOLATED FROM BAL CULTURE		
	FREQ	**%**
FUNGAL ALONE ISOLATED	8	12%
FUNGAL + OTHER ORGANISMS	7	11%
NEGATIVE FOR FUNGAL CULTURE	50	77%
TOTAL	**65**	**100%**

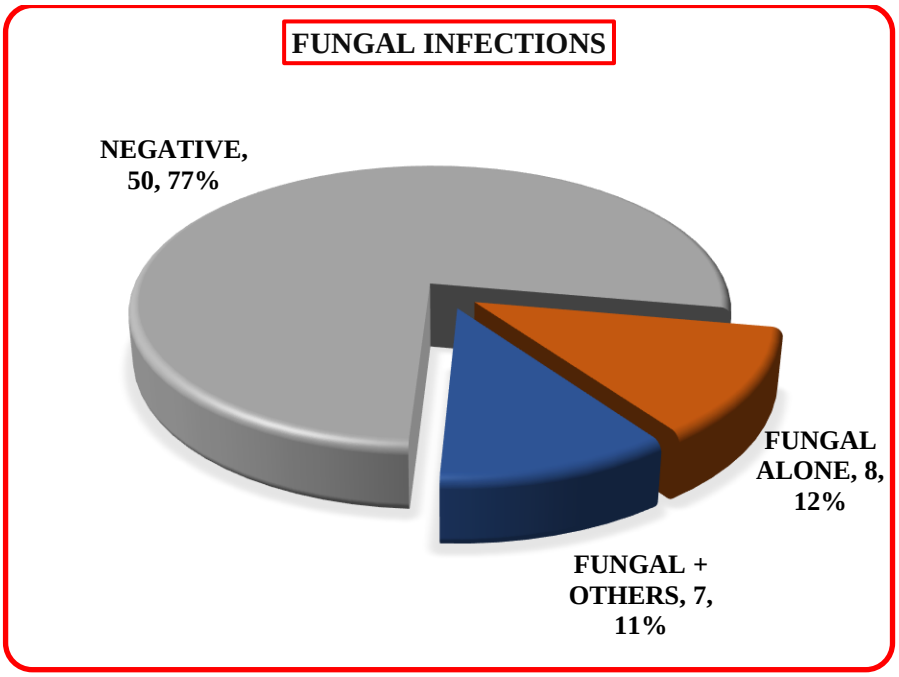


FIG 15: PROPORTION OF FUNGAL INFECTIONS IDENTIFIED BY BAL CULTURE

FUNGAL ORGANISMS GROWN IN BAL FUNGAL CULTURE

TABLE 17: FUNGAL ORGANISMS

FUNGAL ISOLATES IN BAL		
	FREQ	**%**
CANDIDA ALBICANS	2	3%
CANDIDA TROPICALIS	1	1.5%
CANDIDA PARASILOPSIS	1	1.5%
PENICILLIUM MARNEFFI	1	1.5%
ASPERGILLUS NIGER	4	6%
ASPERGILLUS FUMIGATUS	3	4.5%
ASPERGILLUS FLAVUS	2	3%
ASPERGILLUS VERSICOLOR	1	1.5%

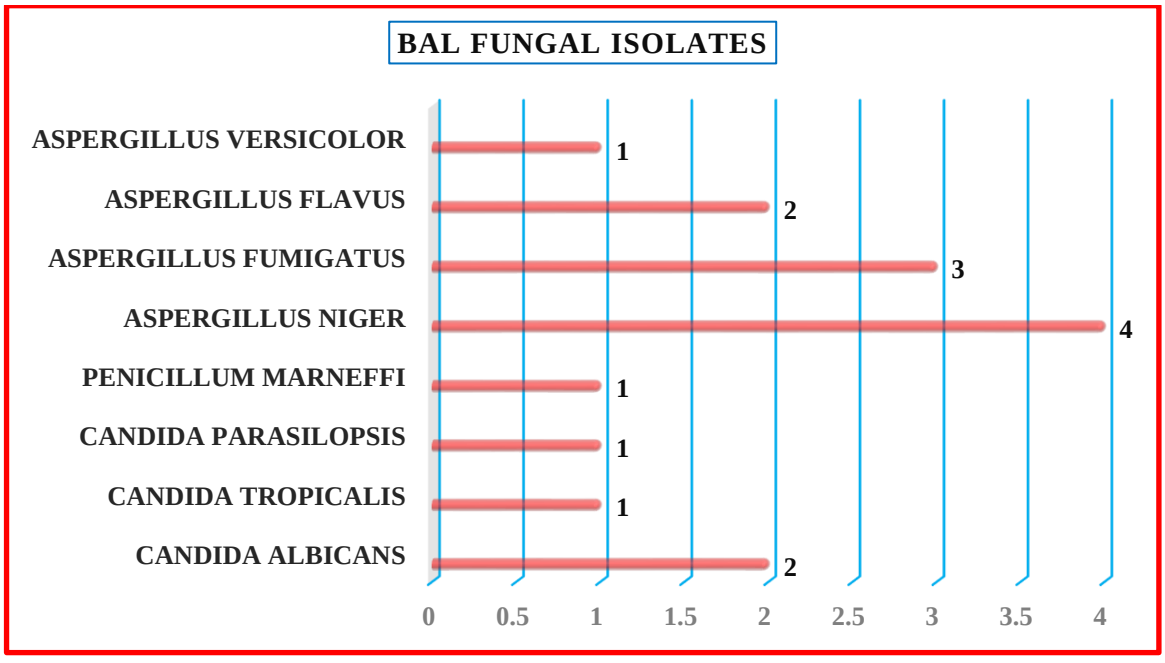


FIG 16: SPECTRUM OF PULMONARY INFECTIONS

PROVEN / PROBABLE FUNGAL INFECTIONS VS COLONISERS

Out of 15 cases of fungal infections diagnosed by BAL culture, Anti-Fungal drugs were started only in 9 patients. The remaining were thought to be due to colonizers in the bronchial tree.

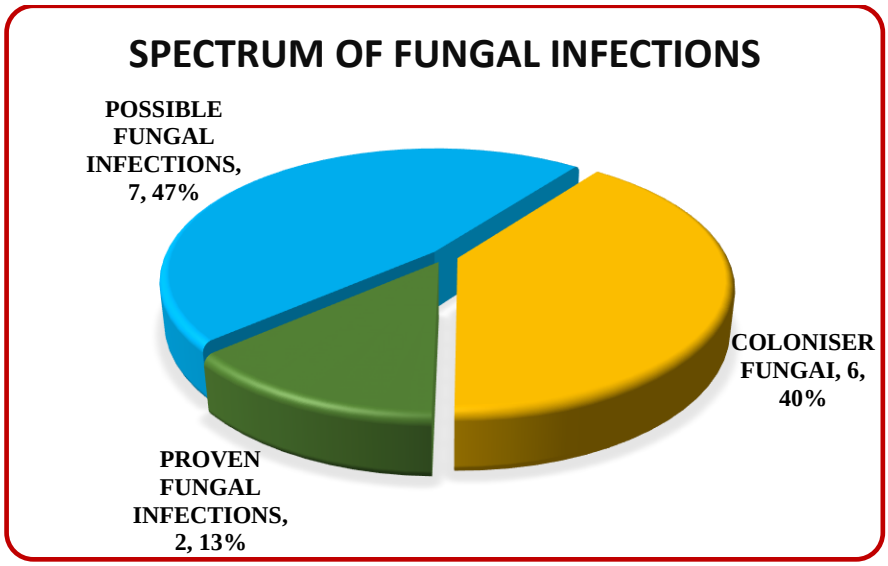


FIG 17: SPECTRUM OF FUNGAL INFECTIONS

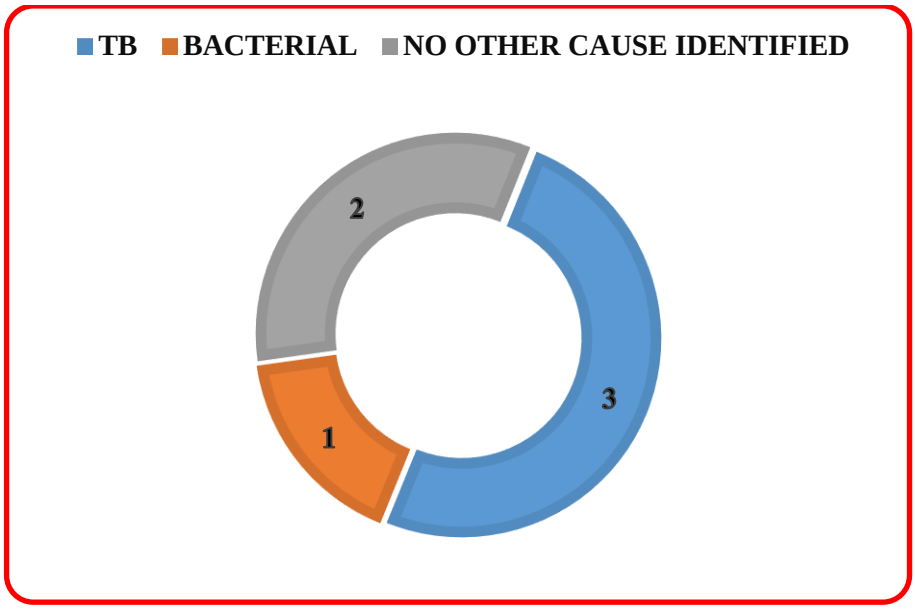


FIG 18: CO-INFECTIONS - FUNGAI ISOLATED AS COLONISERS AS PER DIAGNOSTIC CRITERIA

SPECTRUM OF TUBERCULOUS INFECTIONS

Out of 65 immunocompromised patients, 15 patients BAL GeneXpert MTB was detected, contributing to 24% of pulmonary infections. In 9 patients, tuberculosis alone was detected & and remaining 6 TB was detected with other organisms.

TABLE 18: SPECTRUM OF TUBERCULOSIS

TUBERCULOUS INFECTION DIAGNOSED IN BAL BY GENEXPERT		
	FREQ	**%**
TUBERCULOSIS ALONE	9	14%
TUBERCULOSIS + FUNGAL	2	3%
TUBERCULOSIS + BACTERIAL	4	6%
TUBERCULOSIS + BACTERIAL + FUNGAL	1	1%
NEGATIVE FOR TUBERCULOSIS	50	76%
TOTAL	**65**	**100**

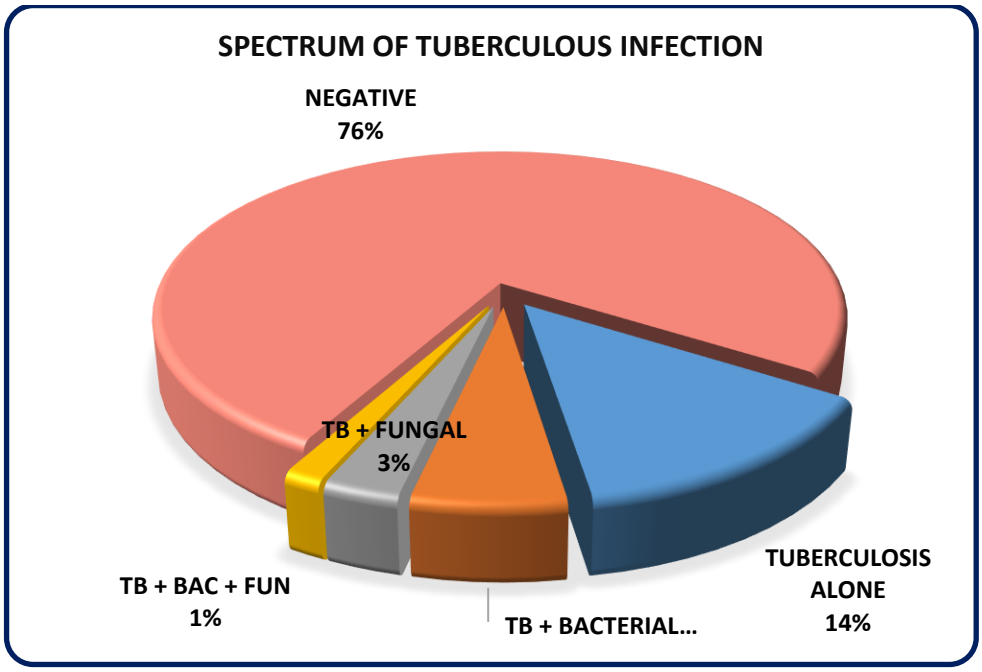


FIG 18: PROPORTION OF PULMONARY TB DETECTED BY BAL

DRUG SENSITIVITY PATTERN AMONG TUBERCULOSIS INFECTION

Out of 15 patients in whom Bronchial Wash GeneXpert MTB was detected 1 showed rifampicin resistant, 1 showed indeterminate pattern, remaining were rifampicin sensitive.

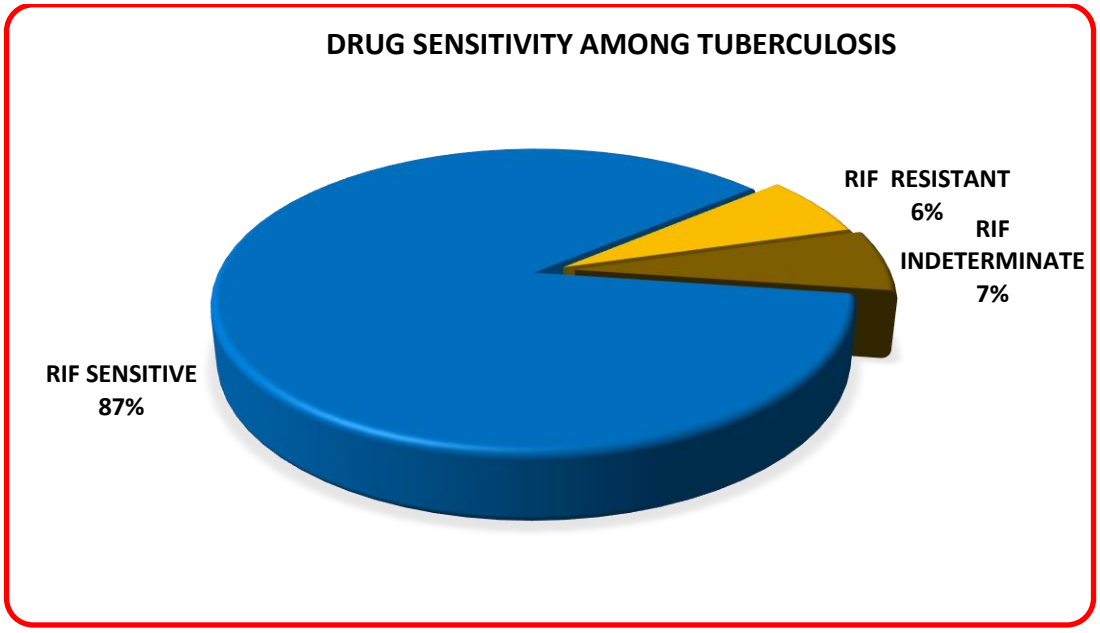


FIG 19: DRUG SENSITIVITY AMONG TUBERCULOSIS PATIENTS.

NON-INFECTIOUS ETIOLOGY DIAGNOSED BY BRONCHOSCOPY

TABLE 19: NON-INFECTIOUS CAUSES

NON-INFECTIOUS CAUSES OF PULMONARY INFILTRATES		
	FREQ	**%**
MALIGNANCY DIAGNOSED BY CYTOLOGY/ HPE	6	9%
HOGKINS LYMPHOMA – LYMPHOMATOUS INFILTRATION	1	1.5%
RADIATION FIBROSIS	1	1.5%
ALVEOLAR HAEMORRHAGE	1	1.5%
INTERSTITIAL FIBROSIS	1	1.5%
TOTAL	**10**	**15%**

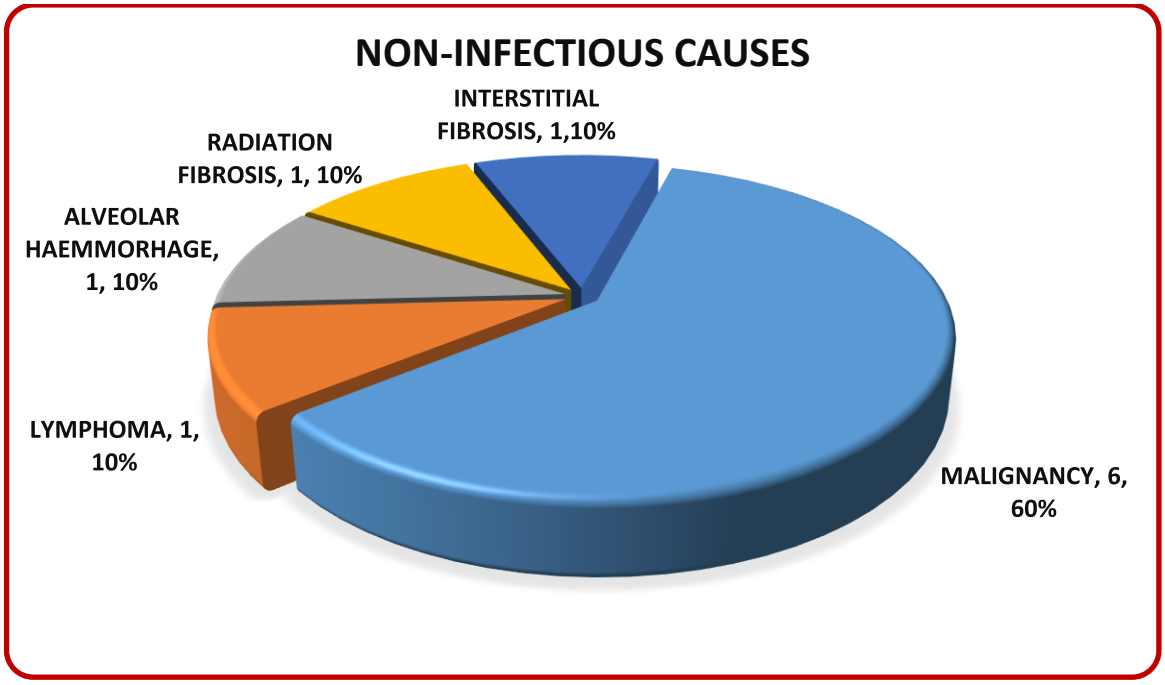


FIG 20: SPECTRUM OF NON-INFECTIOUS CAUSES OF PULMONARY DISEASES

COMPLICATIONS OF BRONCHOSCOPY

Out of 65 immunocompromised patients in whom bronchoscopy was done for evaluation of pulmonary diseases 76% did not have any complications and in remaining 24% minor complications were present.

TABLE 20: COMPLICATIONS OF FOB

COMPLICATIONS OF BRONCHOSCOPY		
	FREQ	**%**
TRANSIENT HYPOXEMIA	10	15%
MINOR BLEEDING	5	8%
PNEUMOTHORAX	1	1%
NO COMPLICATIONS	49	76%
TOTAL	**65**	**100%**

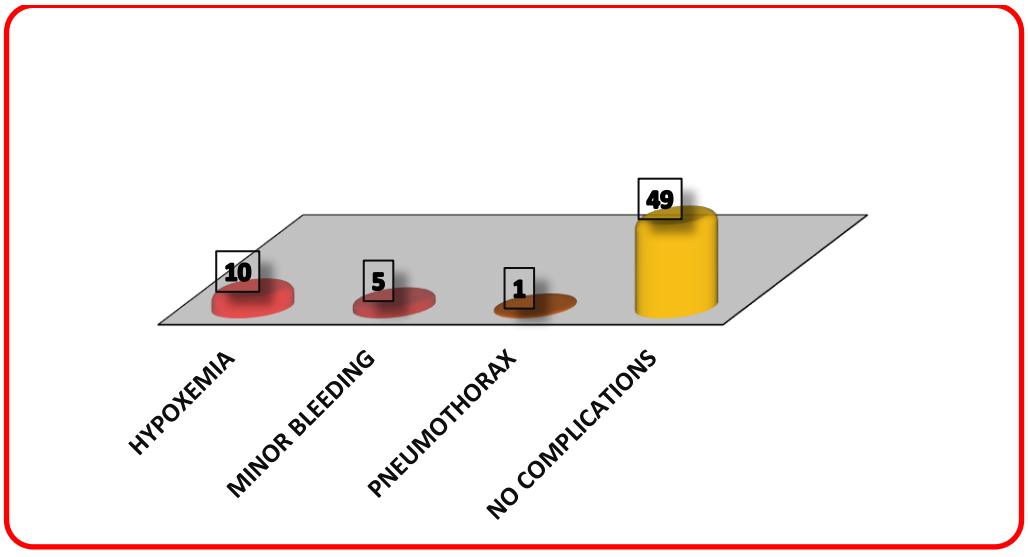


FIG 21: COMPLICATIONS OF BRONCHOSCOPY

CHANGE IN CURRENT EMPERICAL TREATMENT PLAN DUE TO BRONCHOSCOPIC INTERVENTION

Out of 65 immunocompromised patients in whom FOB was done the current treatment plan was changed in 37 patients as the result of bronchoscopic intervention contributing to 57%.

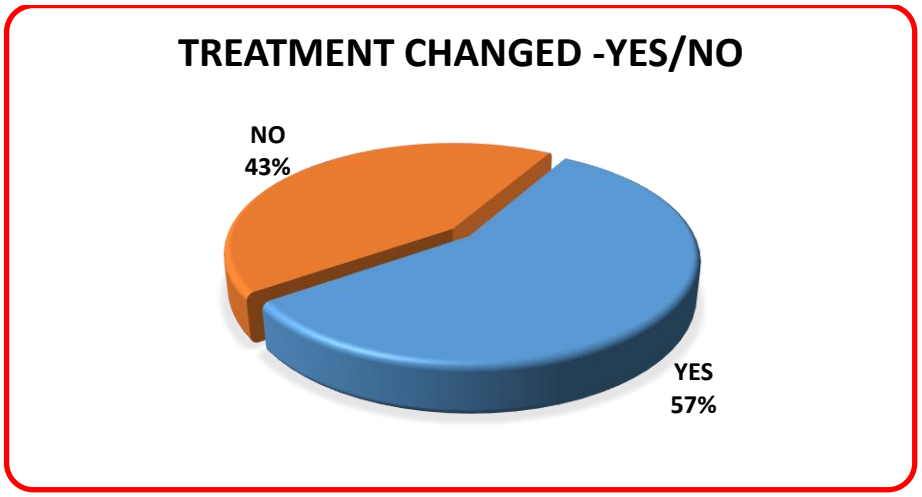


FIG 22: CHANGE IN TREATMENT PLAN AS THE RESULT OF BRONCHOSCOPY

TYPE OF TREATMENT MODIFICATION

TABLE 21: TREATMENT MODIFICATION

TYPE OF TREATMENT MODIFICATION			CLINICAL IMPROVEMENT	
	FREQ	**%**	**IMPROVEMENT**	**%**
ATT STARTED	15	23%	11	75%
ANTIBIOTICS	8	12%	7	90%
ANTIFUNGALS	9	14%	6	65%
CHEMOTHERAPY	5	8%	1	20%
NO CHANGE	28	43%		
TOTAL	**37**	**57%**		

CLINICAL IMPROVEMENT AS THE RESULT OF CHANGE IN EMPIRICAL TREATMENT

Out of 37 patients in whom Bronchoscopy led to change in current treatment plan 26 patients (71%) improved clinically and remaining 11 patients (29%) 4 patients died due to other comorbidities, 4 patients lost follow up and remaining 3 did not improve.

TABLE 22: CLINICAL IMPROVEMENT IN FOLLOW UP

CLINICAL IMPROVEMENT DUE TO CHANGE IN TREATMENT PLAN		
	FREQ	**%**
IMPROVED CLINICALLY	26	71%
DIED DUE TO COMORBIDITIES	4	11%
LOST FOLLOW UP	4	11%
NOT IMPROVED	3	8%
TOTAL	**37**	**100%**

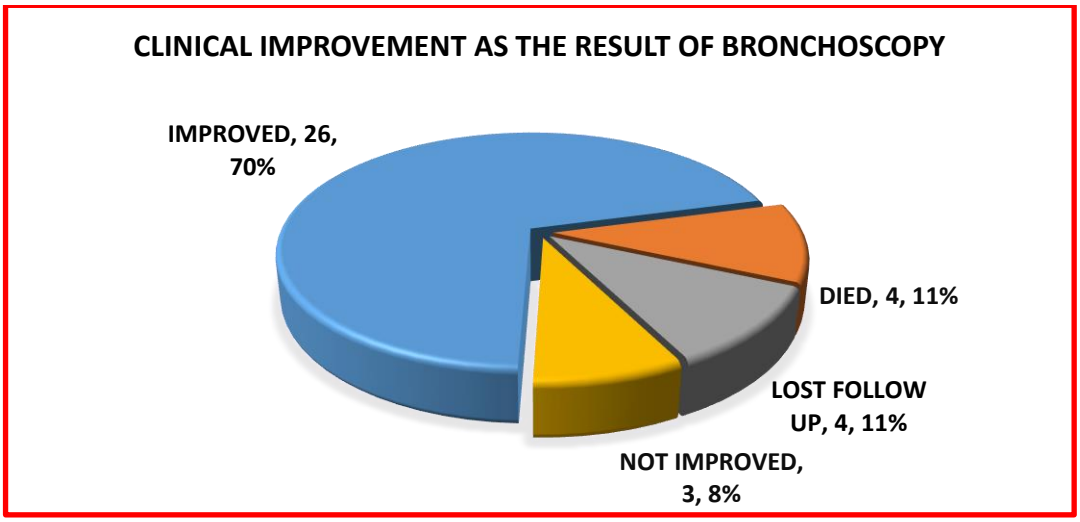


FIG 23: CLINICAL IMPROVEMENT IN DUE TO CHANGE IN EMPIRICAL TREATMENT

BRONCHOSCOPIC EVALUATION OF PULMONARY DISEASES IN NON-HIV IMMUNOCOMPROMIED PATIENTS IN OUR STUDY – THE OVERALL PICTURE

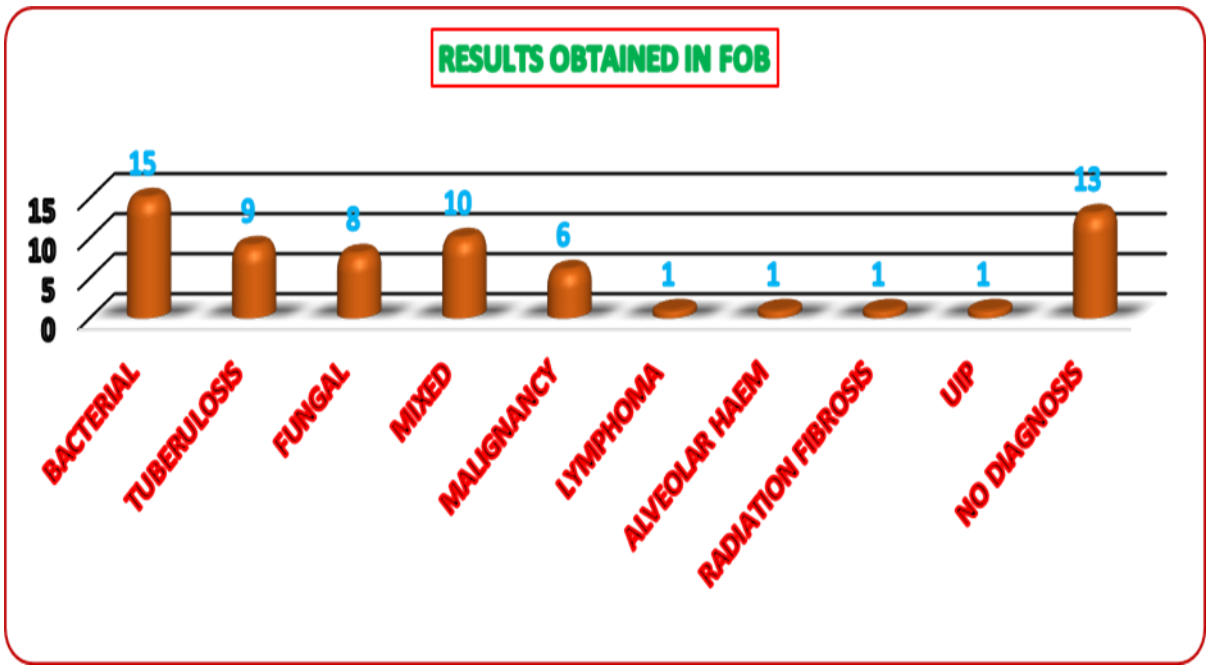


FIG24: BRONCHOSCOPIC EVALUATION OF PULMONARY DISEASES

TABLE 23: OVERALL PICTURE – BRONCHOSCOPIC EVALUATION

BRONCHOSCOPIC EVALUATION OF PULMONARY DISEASES		
	FREQ	**%**
BACTERIAL INFECTIONS ALONE	15	23%
TUBERCULOSIS ALONE	9	14%
FUNGAL ALONE	8	12%
MIXED INFECTIONS/POLYMICROBIAL	10	15%
MALIGNANCY	6	9%
HOGKINS LYMPHOMA INFILTRATION	1	1.5%
RADIATION FIBROSIS	1	1.5%
ALVEOLAR HAEMORRHAGE	1	1.5%
INTERSTITIAL FIBROSIS	1	1.5%
NO DIAGNOSIS	13	20%
TOTAL	**65**	**100%**

COMPARISON OF SYMPTOMS WITH YIELD ON BRONCHOSCOPY

TABLE 24: SYMPTOMS VS YIELD

SYMPTOMS	YIELD ON BRONCHOSCOPY		TOTAL (100%)
	POSITIVE	NEGATIVE	
CHEST SYMPTOMS WITH FEVER	10 (91%)	1 (9%)	11
CHEST SYMPTOMS ALONE	28 (78%)	8 (22%)	36
HAEMOPTYSIS	8 (89%)	1 (11%)	9
FEVER ALONE	6 (100%)	0 (0%)	6
ASYMPTOMATIC	0 (0%)	3 (100%)	3
TOTAL	52	13	65
P VALUE 0.004			

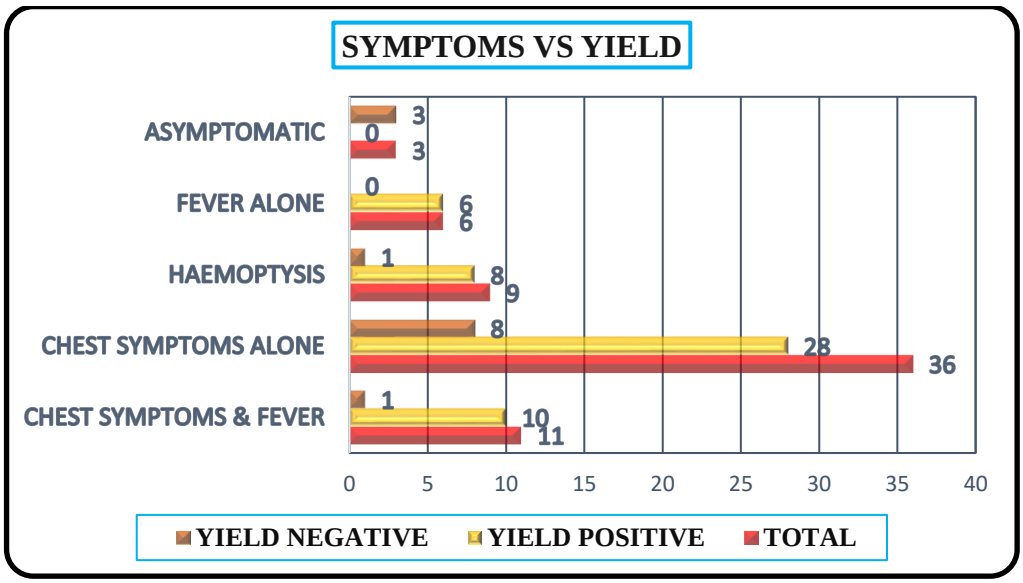


FIG 25: COMPARISON OF SYMPTOMS WITH BRONCHOSCOPIC YIELD

- Fever alone as presenting symptom gave a yield of 100%, followed by chest symptoms with fever with 91%
- So the presence of fever (fever alone or chest symptoms with fever) increased yield to 95% when compared to other symptoms. In asymptomatic patients there was no yield.

COMPARISON OF RADIOLOGICAL PRESENTATION OF BRONCHOSCOPIC YIELD

TABLE 25: RADIOLOGY VS YIELD

RADIOLOGICAL PRESENTATION	YIELD ON BRONCHOSCOPY		TOTAL
	POSITIVE	NEGATIVE	
CONSOLIDATION	27 (87%)	4 (13%)	31
GROUND GLASS PATTERN	7 (78%)	2 (22%)	9
TREE IN BUD PATTERN	3 (75%)	1 (25%)	4
CAVITY	7 (100%)	0 (0%)	7
RETICULAR/NODULAR PATTERN	8 (57%)	6 (43%)	14
TOTAL	52	13	65

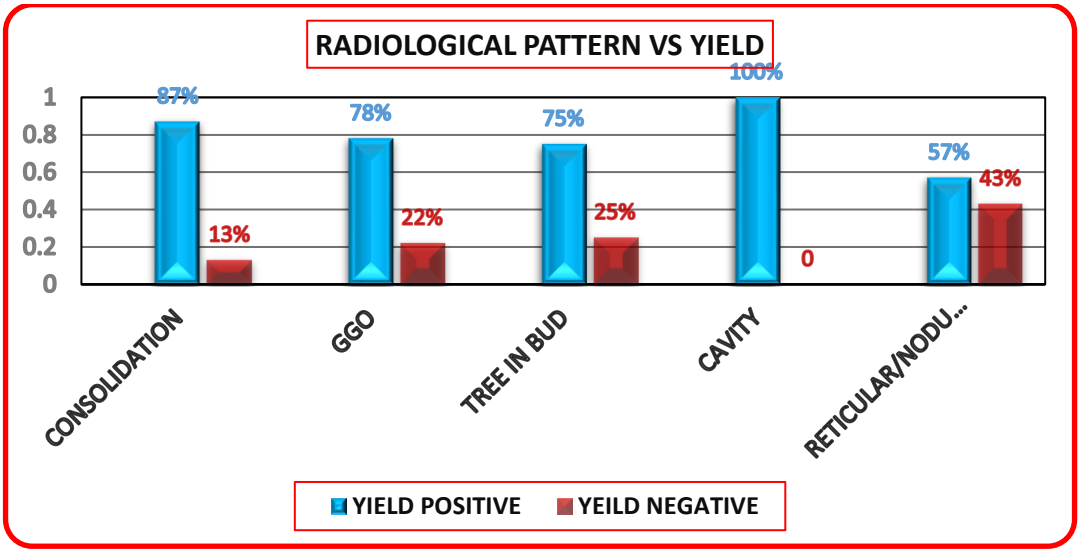


FIG 26: RADIOLOGICAL PATTERN VS YEILD

- Cavity had the highest yield of 100%, followed by consolidation with 87%
- The reticular / Nodular pattern had the lowest yield of 57% out of which 55% were non-infectious and 45% were infectious. Infectious causes were due to 34% tuberculosis and 11% bacterial. Noninfectious causes were malignancy, radiation fibrosis, interstitial pneumonia etc.

COMPARISON OF LOBE INVOLVEMENT IN RADIOLOGY TO YIELD

TABLE 26: LOBE INVOLVEMENT VS YIELD

LOBE INVOLVEMENT	YIELD ON BRONCHOSCOPY		TOTAL
	POSITIVE	NEGATIVE	
UPPER LOBE	20 (95%)	1 (5%)	21
MIDDLE LOBE	12 (70%)	5 (30%)	17
LOWER LOBE	20 (74%)	7 (26%)	27
TOTAL	**52**	**13**	**65**

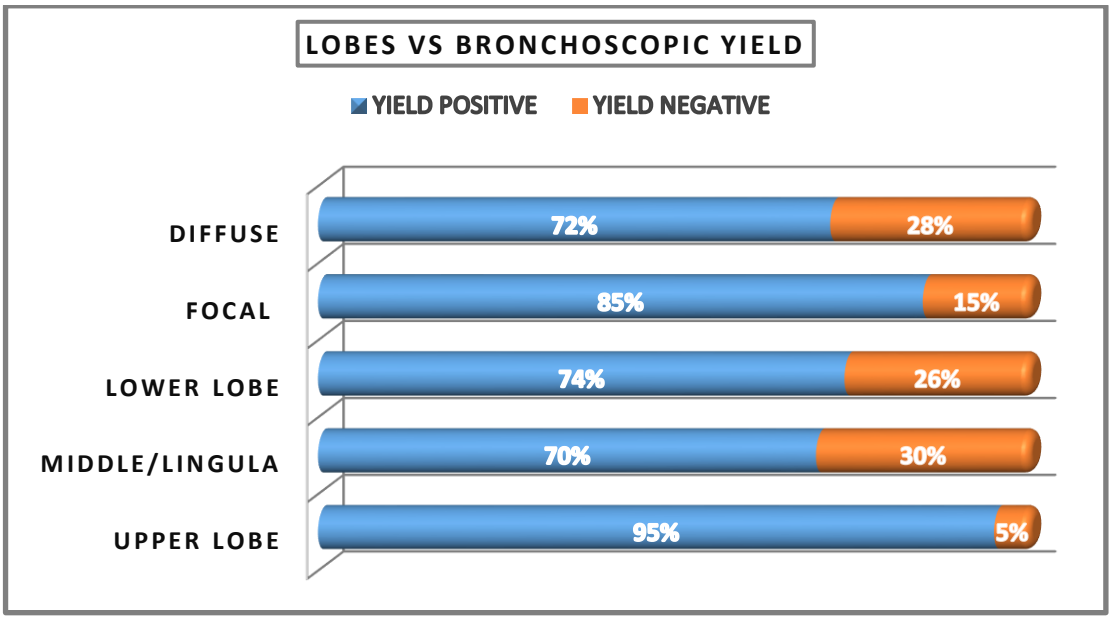


FIG 27: COMPARISON OF LOBE INVOLEMENT TO BRONCHOSCOPIC YIELD

- The upper lobe disease had a better yield of 95% compared to middle & the lower lobe involvement.
- Focal involvement (involvement of one lobe) had a higher yield of 85% when compared to Diffuse disease (2 or more lobes) with 72%

COMPARISON OF YIELD IN BRONCHOSCOPY TO TREATMENT MODIFIED

- 80% (n=52) patients had a positive yield on bronchoscopy.
- Based on bronchoscopy current treatment was modified in 57% (n=37) patients

TABLE 27: YIELD VS TREATMENT MODIFICATION

TREATMENT MODIFIED	**YIELD ON BRONCHOSCOPY**		**TOTAL**
	POSITIVE	**NEGATIVE**	
YES	37 (57%)	0 (0%)	37 (57%)
NO	15 (23%)	13 (20%)	28 (43%)
TOTAL	**52 (80%)**	**13 (20%)**	**65 (100%)**
P VALUE 0.000			

- Out of 65 patients in whom FOB was done the current empirical treatment plan was changed in 37 patients (57%).
- **This was statistically significant with P value of 0.000**

ANALYSIS OF DIFFERENT SUBGROUPS OF IMMUNOCOMPROMISED PATIENTS

GROUP 1: CANCER PATIENTS RECEIVING CHEMOTHERAPY PRESENTING WITH NEW PULMONARY INFILTRATES

- This group contributes to 17% (n=11) of the total population

TABLE 28: SPLIT UP CANCER CHEMOTHERY GROUP

CANCER CHEMOTHERAPY SUBGROUPS		
	FREQ	**%**
LUNG CANCER	1	1.5%
ESOPHAGEAL	2	3%
STOMACH	1	1.5%
PHARYNGEAL	5	8%
BREAST	2	3%

SYMPTOM ANALYSIS

- 55% of patients presented predominantly with chest symptoms
- Presence of fever was less in this group. Only 27% had fever at the time of presentation & remaining 72% was afebrile.

DURATION OF SYMPTOMS

- 18% had acute/short duration of symptoms (< 3 weeks) remaining 72% had symptoms for more than > 3 weeks. When compared to other groups cancer group had longer duration of symptoms possibly because of more non-infectious nature of pulmonary disease.

TABLE 29: DURATION OF SYMPTOMS

DIAGNOSIS	DURATION OF SYMPTOMS				TOTAL
	ASYMPYOMATIC	< 3 WEEKS	3-8 WEEKS	> 8 WEEKS	
CANCER GROUP	0	2 (18%)	4 (36%)	5 (46%)	100%
OTHER GROUPS	3 (5%)	28 (59%)	20 (30%)	3 (6%)	100%
P VALUE	0.001				

RADIOLOGICAL PRESENTATION

- 46% of patients presented with consolidation followed by nodular pattern in 36%.

TABLE 30: RADIOLOGICAL PRESENTATION

DIAGNOSIS	RADIOLOGICAL PRESENTATION						TOTAL
	CONSOLIDATION	CAVITY	NODULAR	RETICULAR	TREE	GGO	
CANCER	5 (46%)	2 (18%)	**4 (36%)**	0	0	0	100%
OTHERS	28 (48%)	5 (9%)	**2 (4%)**	8 (15%)	4 (7%)	9	100%
P VALUE	0.008						

- Nodular involvement in this group was 36% compared to only 4% in other groups. **This was statistically significant with P value 0.008**
- Focal involvement was seen in 82% as against diffuse involvement (2 or more lobes) seen only in 18%.

- Middle lobe/ Lower lobe involvement was seen equally in 36% each, with Upper lobe involvement in 27%.

DIAGNOSIS OF PULMONARY INFILTRATES

In cancer only 36% of pulmonary lesions were infective remaining 64% non-infectious cause. In other groups, non-infectious cause contributed to only 6%. **This was statistically significant with chi-square P value 0.000**

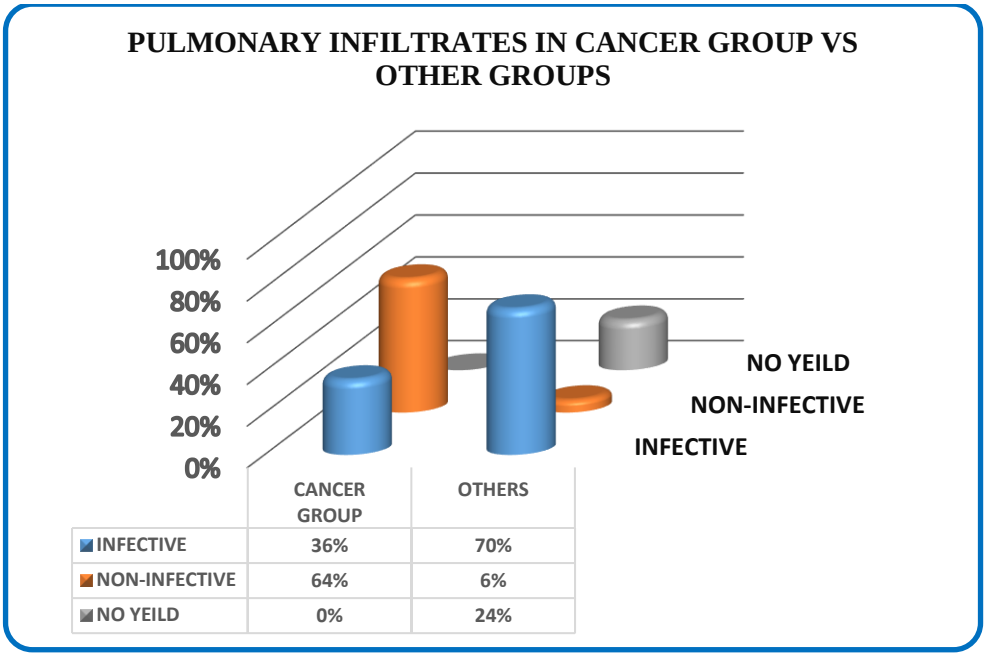


FIG 28: PULMONARY DISEASE IN CANCER GROUP VS OTHER GROUPS

ETIOLOGICAL DIAGNOSIS OF PULMONARY DISEASES.

- Among non-infective causes 54% (n=6) were due to malignancy & 9% (n=1) was due to RADIATION FIBROSIS
- Out of infective etiology TB – 9% (n=1) BACTERIAL – 9 (n=1) & FUNGAL – 18% (n=2) (Aspergillus Niger & fumigatus)

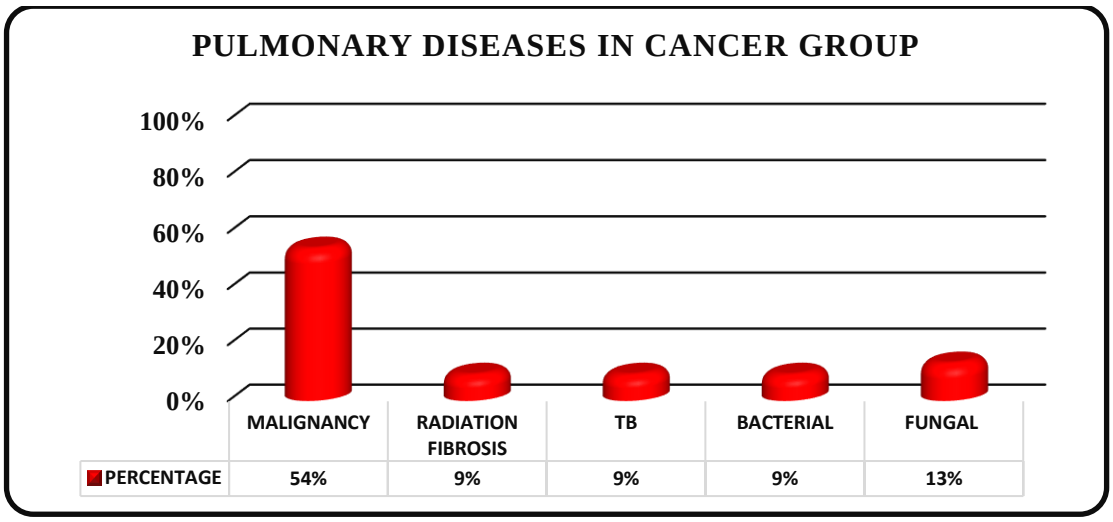


FIG 29: ETIOLOGICAL DIAGNOSIS OF PULMONARY DISEASES IN CANCER GROUP

TREATMENT MODIFICATION & CLINICAL IMPROVEMENT IN CANCER PATIENTS BASED ON BRONCHOSCOPIC RESULTS

- Based on bronchoscopic results, 55% of patients, their current treatment regimen was changed.
- 10%(1 patient) ATT was started, 20%(2 patient) Antifungals started, 27%(3 patient) in whom second line chemotherapy regimens started none improved possibly because of their advanced nature of disease.

  Overall, only 36% patients clinically improved when compared to other groups with 80% clinical improvement with a change in treatment. **This was statistically significant with P value 0.003.** This was because of possible advanced nature of underlying malignancy at time of presentation.

TABLE 30: CLINICAL IMPROMENT CANCER VS OTHERS

DIAGNOSIS	CLINICAL IMPROVEMENT WITH CHANGE IN TREATMENT		
	IMPROVED	NOT IMPROVED	TOTAL
CANCER GROUP	4 (36%)	7 (64%)	11
OTHERS	43 (80%)	11 (20%)	54
P VALUE 0.003			

COMPLICATIONS OF BRONCHOSCOPY

- The most common complication was moderate bleeding due to biopsies.
- Mild to moderate bleeding episodes which was controlled by wedging the bleeding site and applying pressure and instillation of cold saline.
- **Minor bleeding episodes in this group is 27% compared to other groups with 4%, which is statistically significant with P value 0.031**

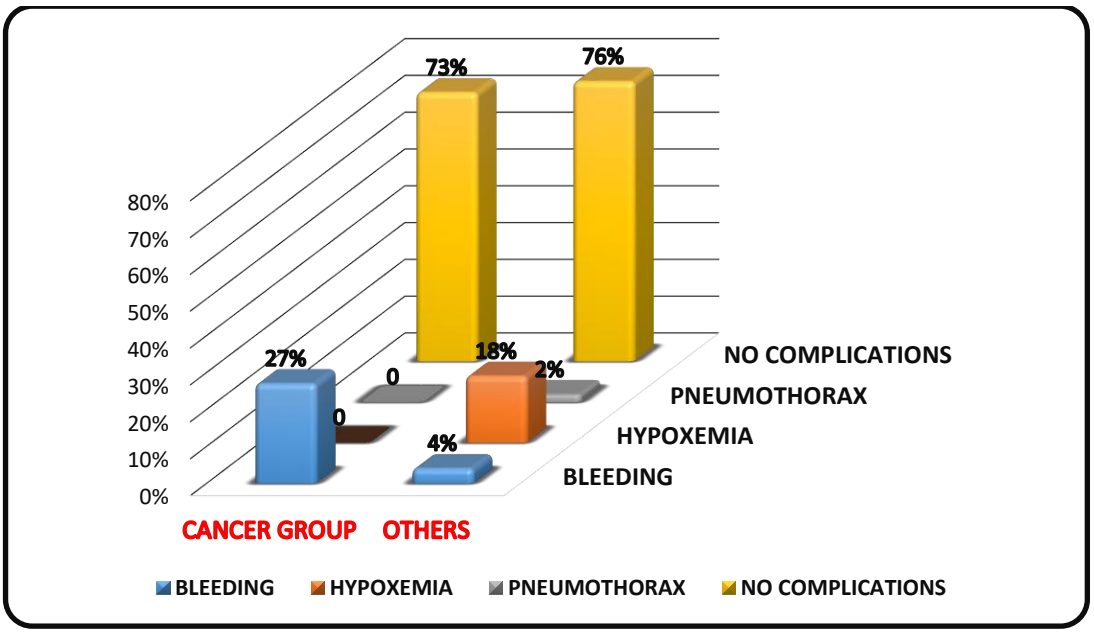


FIG 30: COMPLICATIONS DURING FOB - CANCER GROUP VS OTHERS

GROUP 2: POST RENAL TRANSPLANT PATIENTS RECEIVING IMMUNOSUPPRESIVE DRUGS

- This group contributing to 13.8% (n=9) of the total population

SYMPTOM ANALYSIS

- 67% patients had fever with or without chest symptoms at time of presentation compared to 20% in other groups.
- **This was statistically significant with P value 0.003**

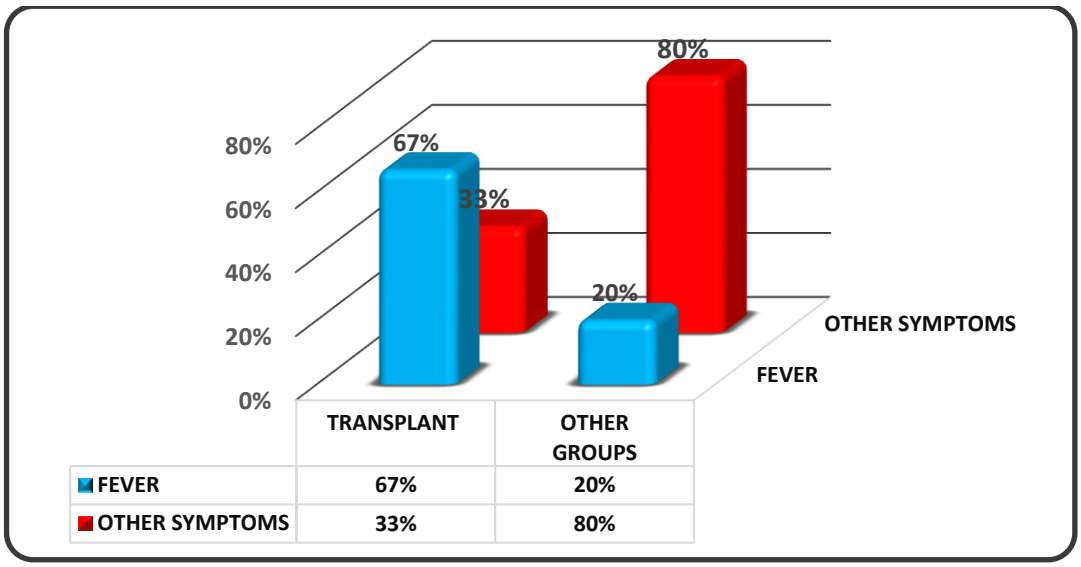


FIG 31: SYMPTOM ANALYSIS – RENAL TRANSPLANT VS OTHER GROUPS

- 89% presented acutely (<3 weeks) of symptoms, only 11% had symptoms more than 3 weeks.

TABLE 31: DURATION OF POST RENAL TRANSPLANT

DURATION OF POST RENAL TRANSPLANTATION	NUMBER
< 1 MONTH	3
1-6 MONTHS	2
> 6 MONTHS	4

RADIOLOGICAL INVOLVEMENT

- 67% presented with a consolidation pattern followed by 22% with GGO pattern**.**
- 55% had predominant lower lobe disease followed by 33% with Upper lobe involvement
- 67% had focal infiltrates and remaining 33% had diffuse disease.

DIAGNOSTIC YEILD OF BRONCHOSCOPY

- Out of 9 patients, 8 had a positive yield (89%) contributing 17% of overall positive yield.

PULMONARY INFECTIONS IN POST RENAL TRANSPLANT GROUP

TABLE 32: SPECTRUM OF PULMONARY INFECTIONS

ETIOLOGY OF PULMONARY INFECTIONS	FREQ	%
NO DIAGNOSIS	1	11%
TUBERCULOSIS	1	11%
FUNGAL	1	11%
BACTERIAL	4	45%
MIXED (BACTERIAL + FUNGAL)	2	22%
NON-INFECTIVE	0	0%
TOTAL	9	100%

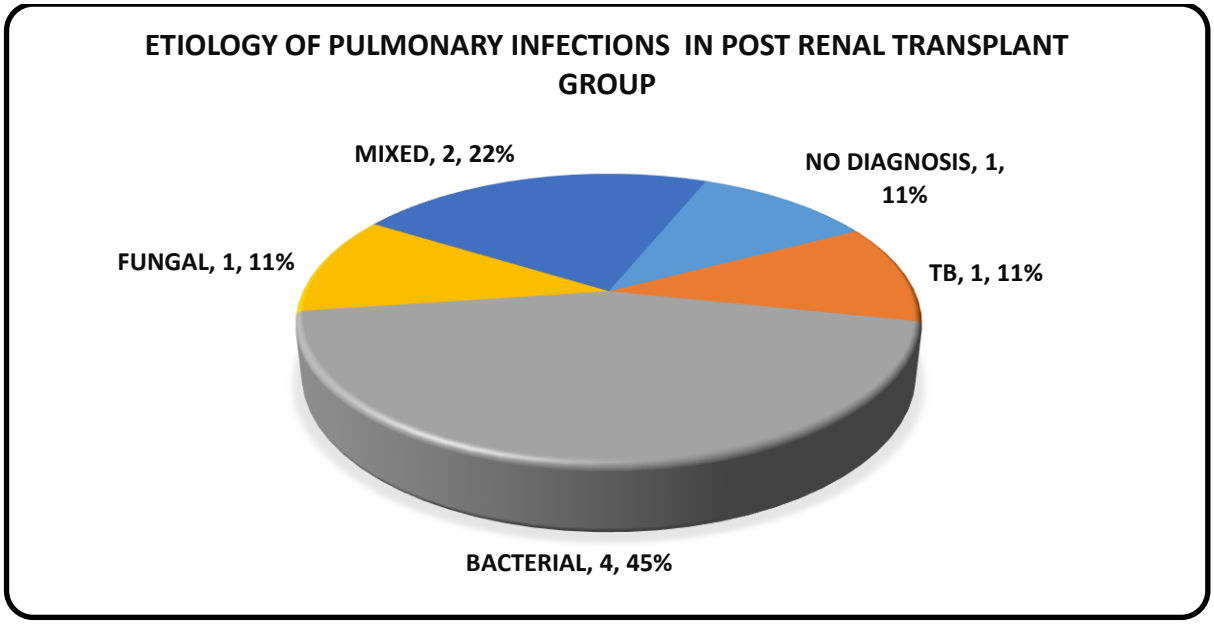


FIG 29: PULMONARY INFECTIONS IN POST RENAL TRANSPLANT GROUP

PULMONARY INFECTIONS IN POST RENAL TRANSPLANT PATIENTS

TABLE 33: ORGANISMS ISOLATED

ORGANISMS ISOLATED	FREQUENCY
KLEBSIELLA SP	1
PSEUDOMONAS SP	2
ACINETOBACTER SP	2
MRSA	1
CANDIDA ALBICANS	1
CANDIDA PARASILOPSIS	1
ASPERGILLUS NIGER	1
TUBERCULOSIS	1

BACTERIAL INFECTIONS IN RENAL TRANSPLANT GROUP COMPARING WITH OTHER GROUPS

Bacterial infections were more common in this group, 67% compared to other groups.

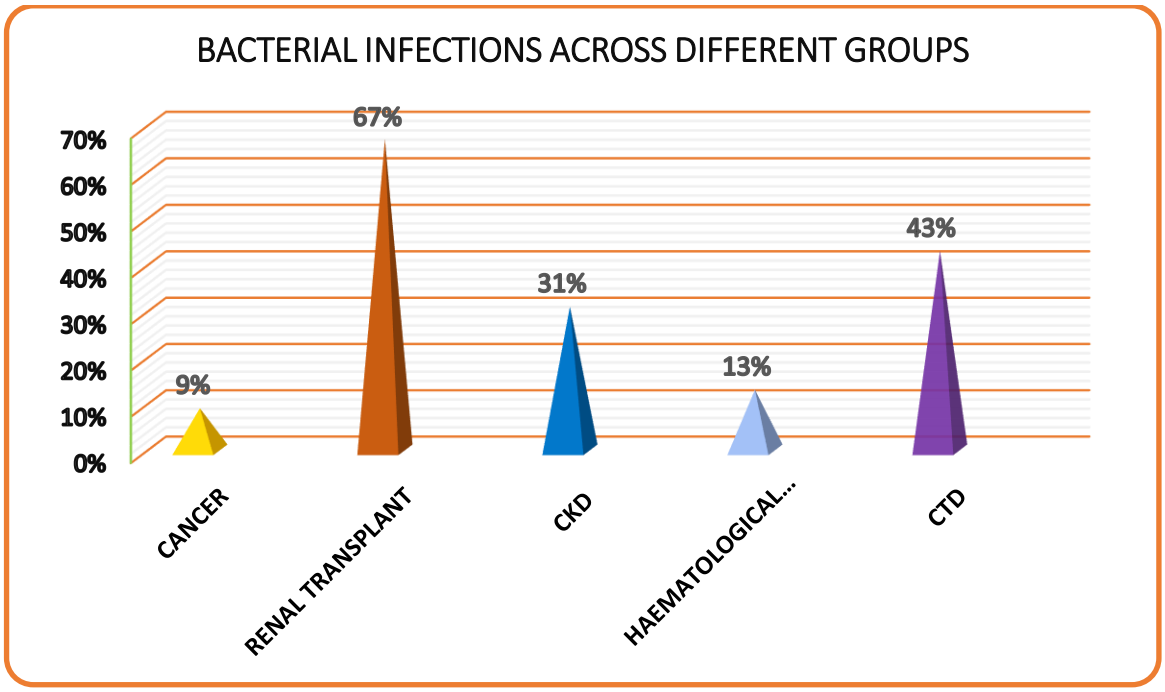


FIG 30: BACTERIAL INFECTIONS ACROSS DIFFERENT GROUPS

SPECTRUM OF PULMONARY INFECTIONS ACCORDING TO DURATION OF POST RENAL TRANSPLANT

TABLE 34: TRANSPLANT DURATION VS PULMONARY INFECTIONS

DURATION OF POST RENAL TRANSPLANT	NO YEILD	TB	BACTERIAL	FUNGAL	MIXED
< 1 MONTH	0	0	2 (67%)	1(33%)	0
1-6 MONTHS	1(50%)	0	1(50%)	0	0
> 6 MONTHS	0	1(25%)	1(25%)	0	2(50%)

- **Immediately POST TRANSPLANT PERIOD (< 1MONTH) bacterial infections are more predominant.**

- **> 6 Months after transplant or after a longer duration of immunosuppression Tuberculosis was more common in our study.**

TREATMENT MODIFICATION AND CLINICAL IMPROVEMENT BASED ON BRONCHOSCOPIC YEILD

- 66% (n=6) of patients, their current empirical treatment modality was changed based on bronchoscopic results. ATT started in 11% (n=1), antibiotics changed in 33% (n=3) antifungals started in 22% (n=2)

COMLICATIONS OF BRONCHOSCOPY

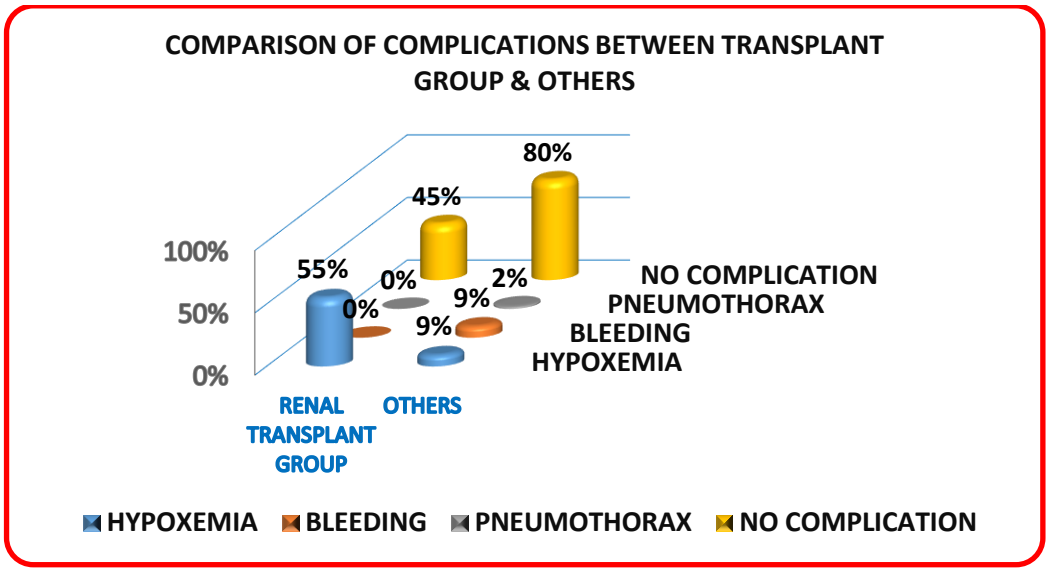


FIG 31: COMPLICATIONS BETWEEN RENAL TRANSPLANT GROUP AND OTHERS

- Overall complications were more in the renal transplant group.

- **Transient hypoxemia was frequently observed (55% vs 9% in the rest). Statistical significance was P value 0.004**

GROUP 3: CHRONIC KIDNEY DISEASE PATIENTS ON MAINTANENCE HAEMODIALYSIS

- This group contributing to 25% (n=16) of the total population studied.
- Bronchoscopic yield was obtained in 69% (n=11) contributing to the overall yield of 21%.

SYMPTOM ANALYSIS IN CKD GROUP

- 62.5% presented with chest symptoms followed by 25% with Haemoptysis.
- Presence of fever was lesser in this group similar to cancer groups
- 63% patients presented with acute symptomatology (< 3 weeks) and remaining 37% with subacute presentation (3-8 weeks).

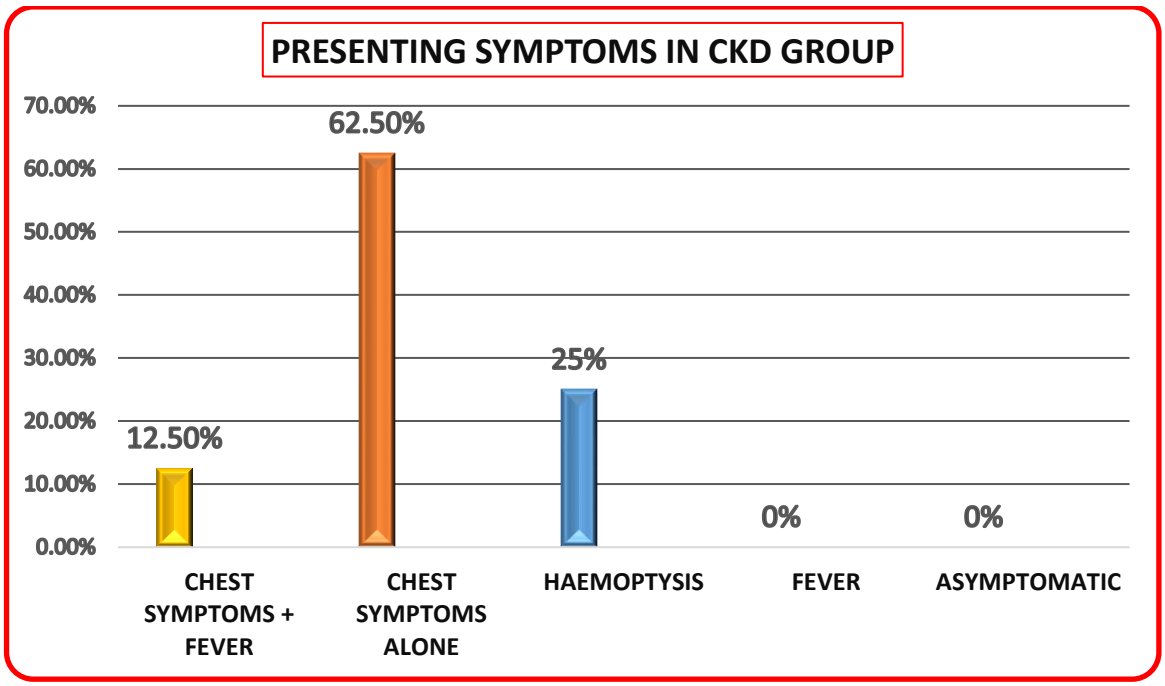


FIG 32: PRESENTING SYMPTOMS IN CKD GROUP

RADIOLOGICAL PRESENTATION

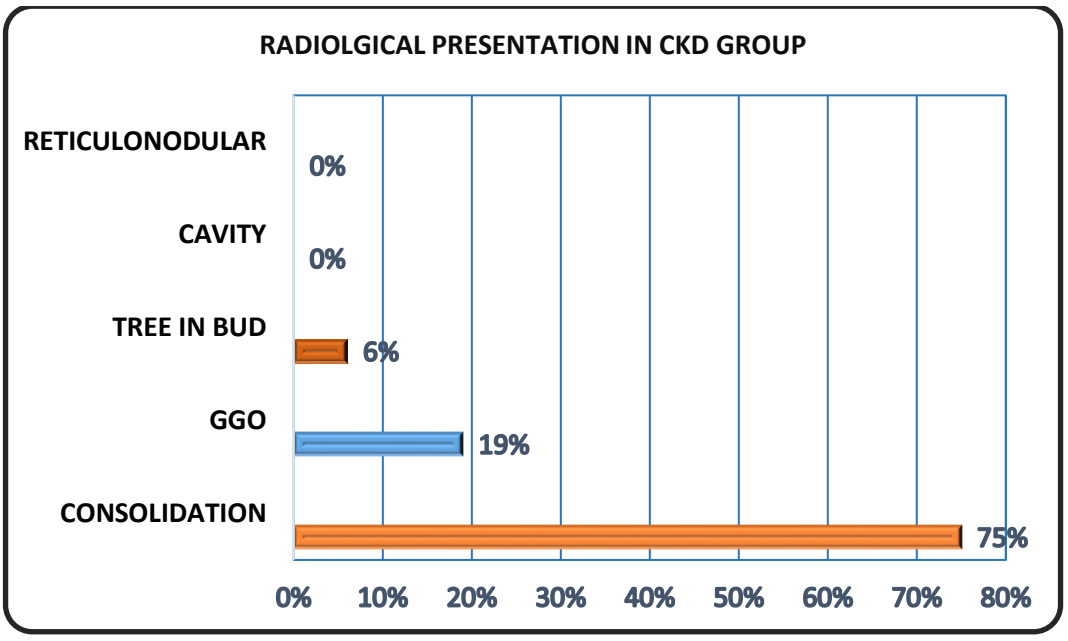


FIG 33: RADIOLOGICAL PRESENTATION CKD GROUP

- The predominant radiological pattern was consolidation occurring in 75%, followed by GGO pattern with 19%.

COMPARISON OF ALVEOLAR PATTERN/ NON-ALVEOLAR PATTERN IN CKD VS OTHER GROUPS.

TABLE 35: RADIOLOGICAL PRESENTATION – CKD VS OTHERS

DIAGNOSIS	RADIOLOGICAL PRESENTATION		
	NON-ALVEOLAR	ALVEOLAR	
CKD GROUP	0	16 (100%)	16 (100%)
OTHERS	14 (29%)	35 (71%)	49 (100%)
TOTAL	14	35	65
P VALUE 0.016			

- **All patients had an alveolar pattern in radiology like when compared to 71% in other groups which was statistically significant with P value 0.016**

DIAGNOSTIC YEILD IN CKD GROUP

- The diagnostic yield in this group was 69% (n=11)
- There were no non-infective causes like in the renal transplant group.

SPECTRUM OF PULMONARY INFECTIONS IN CKD PATIENTS

TABLE 36: PATTERN OF PULMONARY INFECTIONS - CKD

PULMONARY INFECTIONS IN CKD GROUP	FREQ	%
TUBERCULOSIS	2	12%
BACTERIAL	3	19%
FUNGAL	2	13%
MIXED	4	25%
NO DIAGNOSIS	5	31%

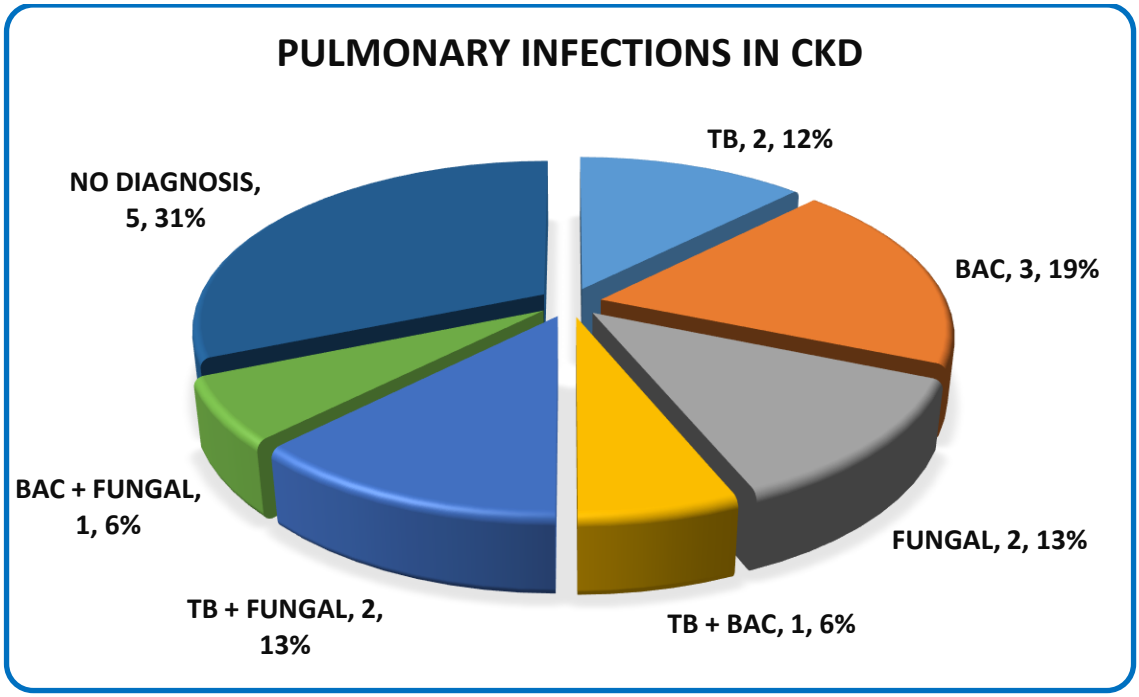


FIG 34: PULMONARY INFECTIONS IN CKD

- Out of mixed infections 3 were due to tuberculosis. (Tuberculosis + Bacteria – 1, Tuberculosis + Fungal – 2, Bacterial + Fungal – 1)

TABLE 37: TYPES OF MICROORGANISMS

MICROORGANISM	FREQUENCY
TUBERCULOSIS	5
KLEBSIELLA SP	2
PSEUDOMONAS SP	1
ACINETOBACTER SP	1
ENTEROCOCCI	1
CANDIDA TROPICALS	1
PENICILLUM SP **[ANNEXURE 2]**	1
ASPERGILLUS NIGER	1
ASPERGILLUS FLAVUS	2

TREATMENT MODIFICATION AND CLINICAL IMPROVEMENT BASED ON BRONCHOSCOPIC YEILD

- Empirical Treatment was modified in 56% (n=9) of patients. Anti-tuberculous therapy started in 30% (n=5), antibiotic regimen changed in 12.5% (n=2) and anti-fungal drug started in 12.5% (n=2).
- 75% (n=6) in whom empirical treatment was modified improved clinically.

COMLICATIONS OF BRONCHOSCOPY

- Overall complications were seen in 37% (n=6) in this group.
- The predominant complication was transient hypoxemia, which required oxygen therapy during and after procedure in 31% (n=5).

GROUP 4: PATIENTS WITH HAEMATOLOGICAL MALIGNANCIES

- This group contributed about 12% (n=8) of the total population.
- Bronchoscopic yield was 75% and contributing to an overall yield of 12%.

TYPES OF HAEMATOLOGICAL MALIGNANCY PATIENTS

TABLE 38: SPLIT UP OF HEMATOLOGICAL MALIGNANCY PATIENTS

DIAGNOSIS	FREQ	%
ACUTE MYELOID LEUKEMIA	4	6%
HODGKINS LYMPHOMA	3	4.5%
NON-HODGKINS LYMPHOMA	1	1.5%

SYMPTOM ANALYSIS

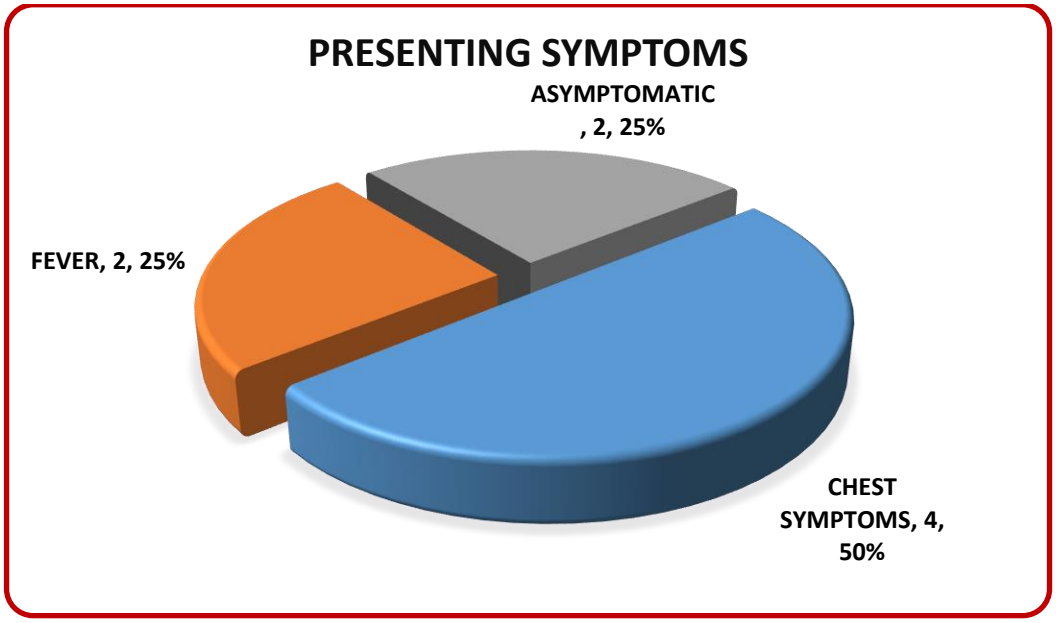


FIG 35: PRESENTING SYMPTOMS IN PATIENTS HAEMTOLOGICAL MALIGNANCY

- Chest symptoms were main presenting symptoms with 50%, followed by 25% with fever & remaining 25% were asymptomatic

RADIOLOGICAL PRESENTATION

- 63% presented with an alveolar pattern (consolidation, GGO, cavity)
- Upper lobe involvement was seen in 62.5% with Middle lobe/Lingular involvement in 25% and Lower lobe involvement in 12.5%.
- Focal involvement was seen in 87.5% and Diffuse involvement 12.5%.

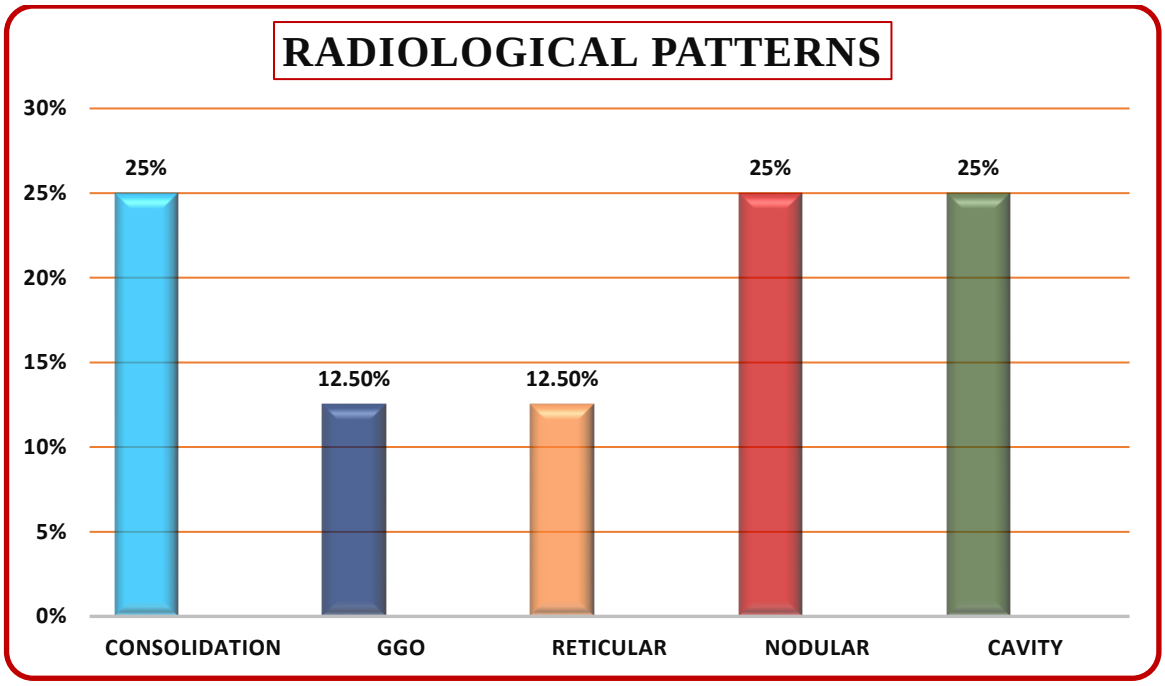


FIG 36: RADIOLOGICAL PATTERNS IN HAEMATOLOGICAL MALIGNACY GROUP

DIAGNOSTIC YIELD

- A positive diagnostic yield is FOB was obtained in 75% (n=6)
- 62.5% (n=5) were infectious and 12.5% (n=1) were non-infectious.
- The noninfectious case was a Lymphomatous infiltration in a patient with Hodgkin's Lymphoma presenting with right upper lobe consolidation, which was proven by Trans Bronchial lung biopsy [**refer Annexure 1**]

SPECTRUM OF PULMONARY INFECTIONS

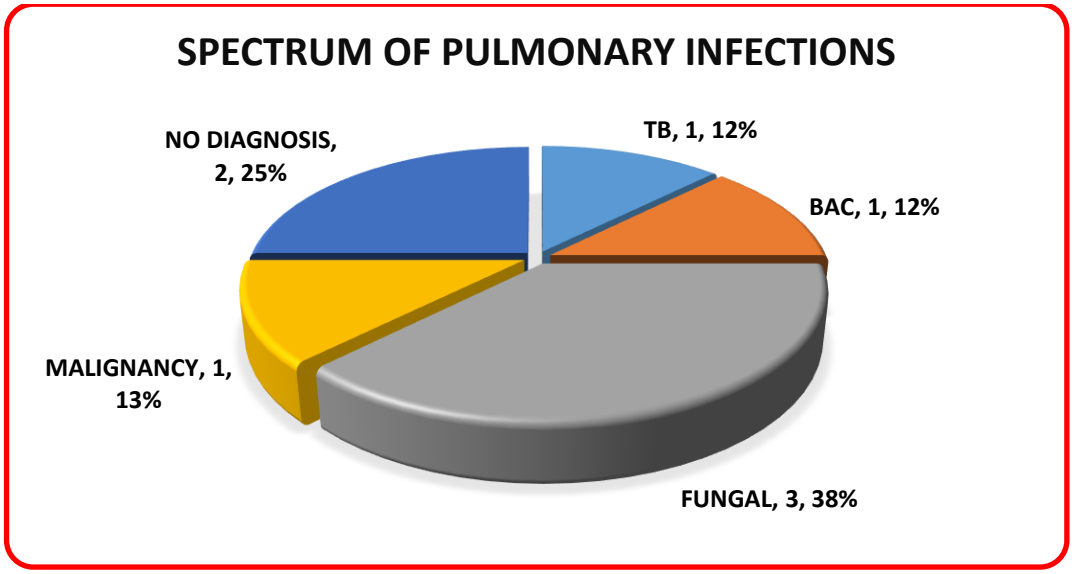


FIG 37: PULMOARY INFECTIONS IN HAEMATOLOGICAL MALIGNANCY

TABLE 39: ORGANISMS IDENTIFIED – HEMATOLOGICAL MALIGNANCY

ORGANISMS	FREQUENCY
KLEBSIELLA SP	1
ASPERGILLUS NIGER	1
ASPERGILLUS FUMIGATUS	1
CANDIDA ALBICANS	1
TUBERCULOSIS	1

TREATMENT MODIFICATION AND CLINICAL IMPROVEMENT BASED ON BRONCHOSCOPIC RESULTS

- Treatment was modified in 50% (n=4) based on bronchoscopic results. ATT started in 12.5% (n=1), anti-fungal started in 25% (n=2), chemotherapy restarted in 12.5% (n=1). All patients in whom treatment was modified based improved clinically

GROUP 5: CONNECTIVE TISSUE DISEASE (CTD) PATIENTS ON CORTICOSTEROIDS/IMMUNOSUPPRESIVE DRUGS/BIOLOGICAL AGENTS

- This group constituted around 32% (n=21) of the total studied population.
- 71% (n=15) patients had a positive yield on bronchoscopy contributing to the overall yield of 28%.

SUBTYPES OF CONNECTIVE TISSUE DISEASE PATIENTS

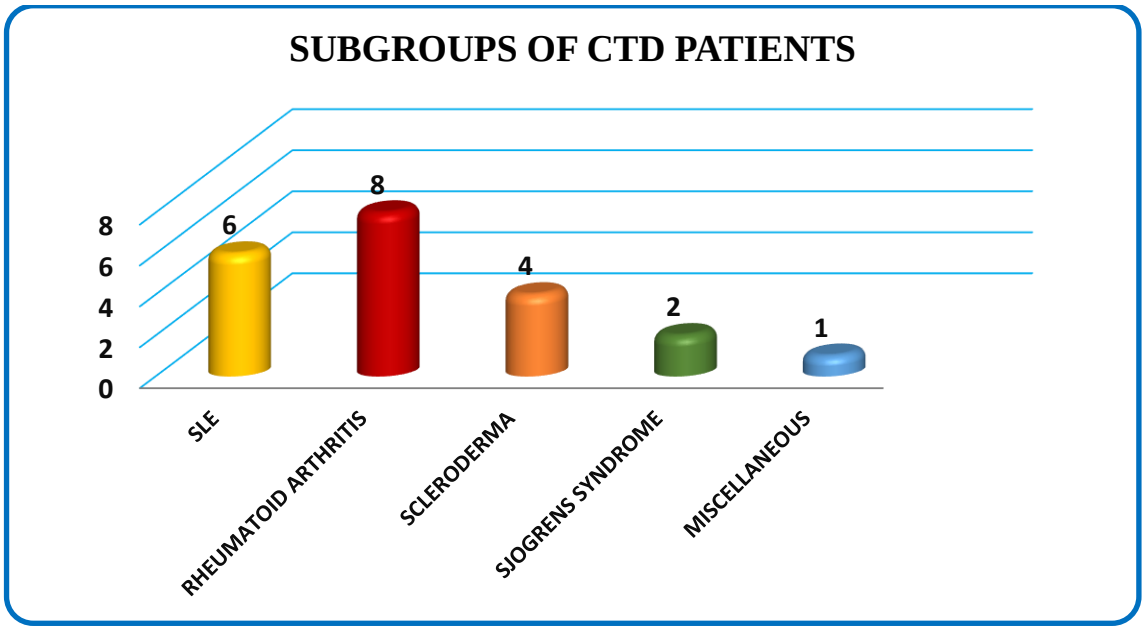


FIG 38: SUBGROUPS OF CONNECTIVE TISSUE DISEASE PATIENTS

TYPES OF IMMUNOSUPPRESIVE DRUGS RECEIVED

- **CORTICOSTEROIDS:** Patients received Prednisolone at a dose of > 20 mg/day on a long term basis, at least for a period of more than 4 weeks.
- OTHER IMMUNOSUPPRESIVE DRUGS: Includes patients receiving a combination of immunosuppressive drugs like weekly doses of Methotrexate/ Daily doses of Azathioprine/ Daily doses of Mycophenolate Mofetil/

Cyclophosphamide on intermittent monthly doses along with or without corticosteroids.

- **BIOLOGICAL AGENTS:** Three patients received RITUXIMAB a monoclonal antibody against anti CD 20 for treatment of Rheumatoid Arthritis.

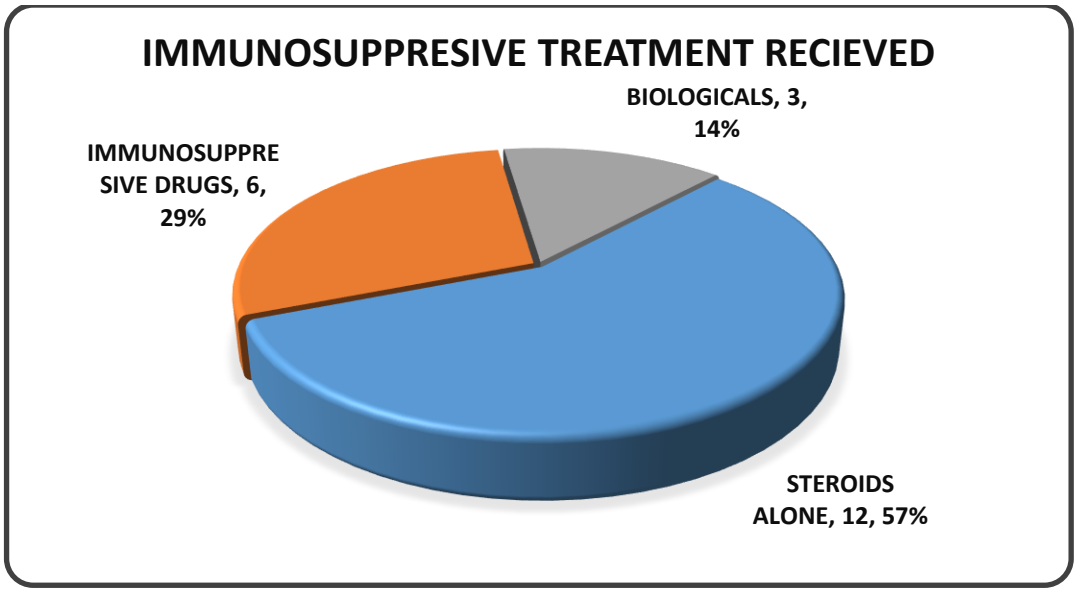


FIG 39: TYPES OF IMMUNOSUPPRESIVE DRUGS RECEIVED

SYMPTOM ANALYSIS

- Most patients presented with chest symptoms like breathlessness, dry cough, because of the predominant pulmonary interstitial lung disease.
- Presence of fever was less common in this group
- Only 19% had fever with or without chest symptoms at time of presentation as compared to 81% who did not have fever, possibly because of high level of immune suppression induced by drugs.

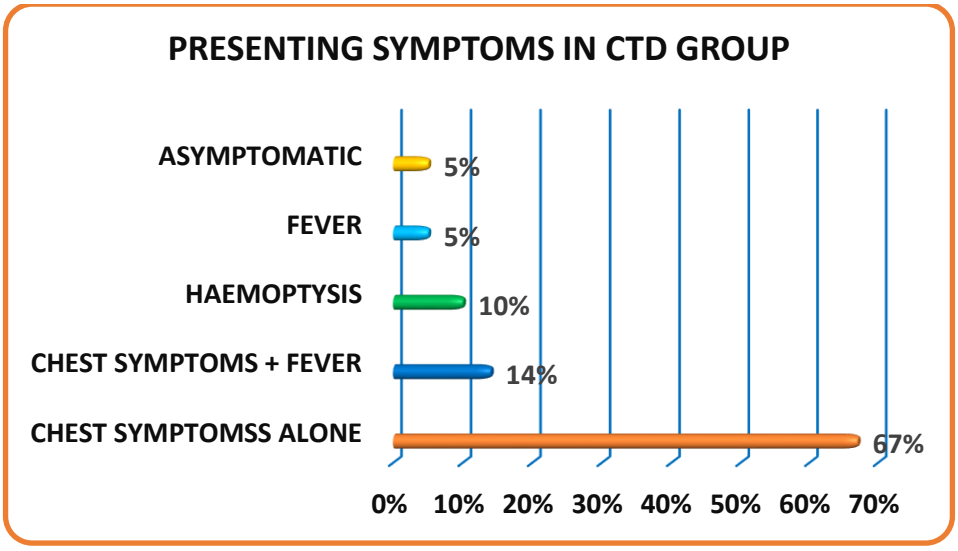


FIG 40: SYMPTOMS IN CTD PATIENTS

DURATION OF SYMPTOMS

TABLE 40: SYMPTOM DURATION - CTD

DURATION	PERCENTAGE
ASYMPTOMATIC	5% (1)
0-3 WEEKS	52% (11)
3-8 WEEKS	33% (7)
> 8 WEEKS	10% (2)

- More than 50% of patients had an acute presentation with symptoms of < 3 weeks duration. Remaining 43% had longer duration of symptoms and 5% were asymptomatic referred with lesion in chest radiography.

RADIOLOGICAL PATTERN IN CTD GROUP

- The most common radiological pattern in this group is the reticular pattern due to the presence of underlying interstitial lung disease.

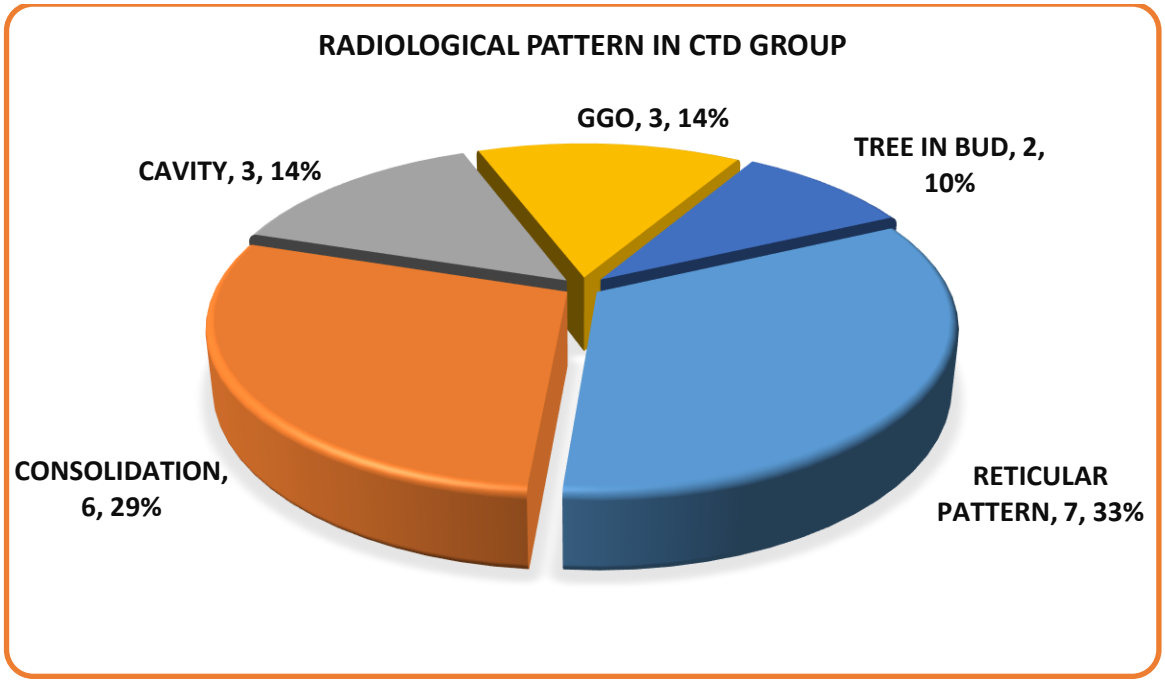


FIG 41: RADIOLOGICAL PATTERNS IN CTD GROUP

TABLE 41: RADIOLOGICAL PATTERN CTD VS OTHERS

DIAGNOSIS	RADIOLOGICAL PATTERN					
	CONSOLIDATION	CAVITY	GGO	NODULAR	RETICULAR	TIB
CTD GROUP	29% (6)	14% (3)	14% (3)	0%	33% (7)	10%
OTHERS GROUPS	57%	10%	14%	14%	2%	5%
P VALUE 0.004						

LOBE INVOLVEMENT IN CTD GROUP

- Lower involvement was most common 43%, followed by upper lobe 21%, Middle lobe/Lingular involvement in 17%
- Focal involvement was seen in 52% and diffuse involvement in 48%.

TABLE 42: LOBE INVOLVEMENT CTD VS OTHER GROUPS

DIAGNOSIS	LOBE INVOLVEMENT	
	FOCAL	DIFFUSE
CTD GROUP	52%	48%
OTHER GROUPS	81%	18%
P VALUE 0.013		

- **In CTD group diffuse disease is more common than other groups (48% vs 18%). This was statistically significant P value 0.013.**

SPECTRUM OF PULMONARY DISEASES IN CTD GROUP

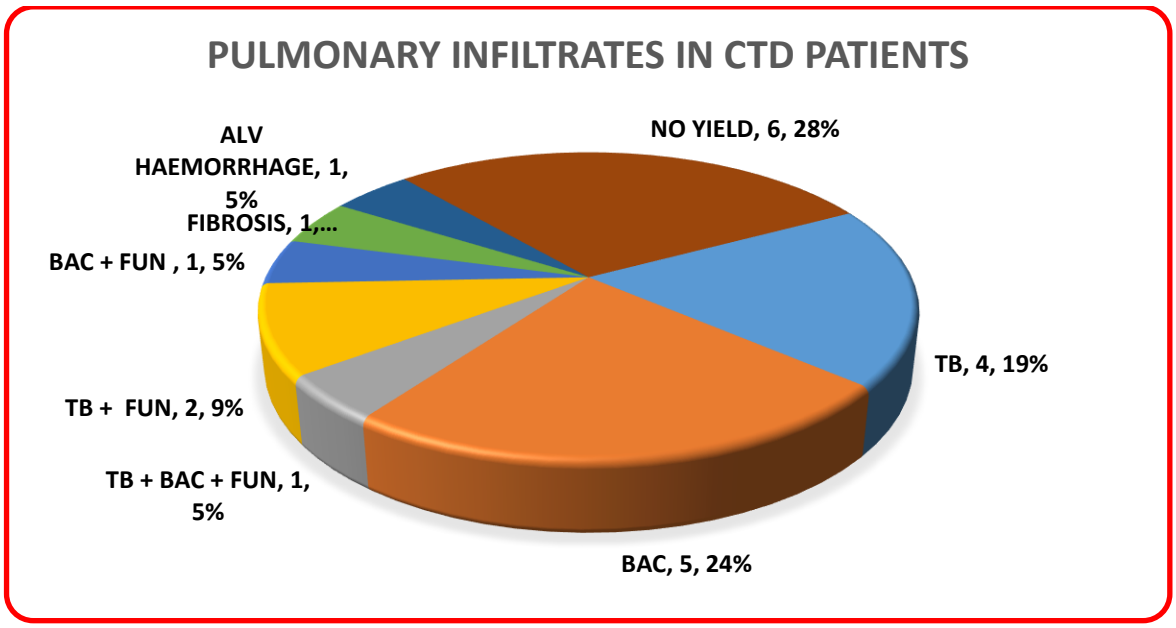


FIG 42: PULMONARY INFILTRATES IN CTD GROUP

TABLE 43: SPECTRUM OF PULMONARY DISEASES - CTD

PULMONARY DISEASES	FREQUENCY
TUBERCULOSIS ALONE	19% (4)
BACTERIAL ALONE	24% (5)
MIXED INFECTIONS	19% (4)
INTESTITIAL FIBROSIS	5% (1)
ALVEOLAR HAEMORRHAGE	5% (1)
NO YIELD	28% (6)

TABLE 44: MICROORGANISMS ISOLATED AND THEIR FREQUENCY

MICROORGANISM	FREQUENCY
PSEUDOMONAS SP	3
MRSA	3
ENTEROCOCCI	1
E. COLI	1
PSEUDOMONAS + MRSA	1
ASPERGILLUS FUMIGATUS	1
ASPERGILLUS VERSICOLOR	1
TUBERCULOSIS	**7**

COMPLICATIONS OF BRONCHOSCOPY

- 95% of patients did not have any complications.
- The only one complication was due to pneumothorax, which developed during Trans Bronchial Biopsy, which needed ICD insertion.
- **Overall complications in this were less when compared to other groups.**

DISCUSSION

Sixty-five Non-HIV immunocompromised patients with pulmonary diseases were studied. They were divided into 5 groups, namely Cancer chemotherapy group, Post Renal Transplant Group, Chronic Kidney Disease on Haemodialysis, hematological malignancies & Connective tissue diseases on immunosuppresants.

The main goal of our study was to evaluate the diagnostic utility of early bronchoscopy in non-HIV immunocompromised patients and the therapeutic utility in terms of treatment modification and clinical improvement as the result of bronchoscopic intervention.

This is the first kind of study done in of Non-HIV immunocompromised population at our tertiary care hospital. The purpose of doing the study was because of lack of Studies done in our Indian population on bronchoscopic evaluation of pulmonary diseases especially in Non-HIV immunocompromised patients. Studies are only available in different subgroups like hematological malignancies, CKD, renal transplant recipients etc. With better chemotherapeutic drug availability for management of malignancies, well-functioning organ transplant programs, increased use of potent immunosuppresive drugs and newer biological agents for managing connective tissue diseases, more people are made immunocompromised for therapeutic reasons for management of their primary diseases. Ultimately more and more patients are developing pulmonary diseases

and the number of referrals are being increased to the Pulmonology department for their management.

Most of these patients are already been treated empirically with multiple potent antimicrobial drugs before being our Pulmonary medicine department. There is also increasing demand from other departments to start empirical Antituberculosis Treatment once patient does not improve with empirical antimicrobial therapy. Even some of the non-infectious causes like pulmonary edema, alveolar hemorrhage, malignancy are misdiagnosed and treated as infectious empirically. Because of this empirical treatment approach, there is increased economic burden, toxicity of antimicrobial therapy, increased incidence of multidrug resistant organisms and delay in starting proper treatment. This study highlights the role of early bronchoscopy in immunocompromised patients with pulmonary diseases that are not improving with empirical treatment with regards to its diagnostic yield, safety and change in empirical treatment. Patients were also followed up to look for clinical improvement.

AGE DISTRIBUTION

The mean age of the patients was 41.91 with a standard deviation of 15.5. The age of patients ranged from 15 years – 74 years. The patients were equally divided among two age groups < 40 years & > 40 years with 51% and 49% respectively. The bronchoscopic yield was almost similar in both age groups with 81% in < 40 years and 78% in > 40 years. There was no statistical difference in yield, symptomatology, radiology or infections in both groups.

GENDER DISTRIBUTION

Out of 65 patients included in study 36 were male and 29 were females. Thus, ratio was 55% & 45% male to female**.**

SYMPTOMATOLOGY

Chest symptoms alone were the most common presentation with 55%, followed by chest symptoms along with fever in 17%. 5% of patients were asymptomatic. Presence of fever gave a higher overall yield of 95%. In asymptomatic patients, yield was zero**. The statistical significance in chi-square P value was 0.004.**

Kyle R. Brownback et al., [55] observed similar finding where the diagnostic yield was significantly improved in the presence of fever.

DURATION OF SYMPTOMS

52% of patients presented with acute symptoms < 3 weeks, followed by 31% with symptoms 3-8 weeks duration and 12% with > 8 weeks duration. 5% were asymptomatic. Cancer chemotherapy group had longer duration of symptoms (72% with symptoms > 3 weeks duration) at the time of presentation. Post renal transplant (89%) & CKD patients (69%) more often had shorter duration of symptoms (< 3 weeks). **The statistical significance was P value < 0.05.** The reason for more acute presentation in renal transplant and CKD group is because the pulmonary diseases were more of infectious etiology especially bacterial. In cancer group the disease process was mainly malignant infiltration hence fever was absent and they presented more gradually.

RADIOLOGICAL PATTERNS

Consolidation was the predominant pattern seen in 48%, followed by GGO with 14%, reticular pattern 12%, cavity 11%, nodular 9% and tree in bud 6%. Cavitary disease had a maximum yield of 100%, followed by consolidation with 87%. Reticular pattern had the lowest yield of 57%. Yield was better in an alveolar pattern of involvement in radiography.

Kyle R. Brownback et al., [55] & Danes et al [33]., in their study also had similar findings, unilateral & alveolar pattern in radiography had a better diagnostic yield.

LOBE INVOLVEMENT

Lower lobe involvement was most common with 41% followed by upper lobe with 32% and middle lobe/lingula with 26%. Focal involvement (single lobe) was more common with 78%. Yield was better in upper lobe involvement & focal involvement with 95% & 85% respectively.

YIELD OF BRONCHOSCOPY

The overall yield of bronchoscopy in our study was 80% with no diagnosis obtained in remaining 20%. 65% were due to infectious causes and 15% were due to non-infectious etiology. Similar studies done in immunocompromised patients have shown wide variations in overall yield ranging from 50-80%. But in most of the studies yield has been high for an infectious etiology ranging from 60-80% similar to our study.[33,34,56, 57]

In a similar study done by Jain, P et al., [58] in 104 Non-HIV immunocompromised patients, the overall yield was 56.2% with high yield for an infectious etiology with 81%.

A similar study done in the Indian population of Menon LR, et al., [59]. He studied 16 renal transplants, 14 dialysis, 8 HIV positive patients, and the clinical utility of BAL in diagnosis of pulmonary infections. The overall yield was 76% of all the three groups put together. BAL cytology had a better yield when compared to culture.

SPECTRUM OF PULMONARY INFECTIONS

Our study results showed that in our tertiary care hospital among the immunocompromised patients bacterial infections were the predominant cause of pulmonary infections (35% overall, 23% by bacterial alone and 12% of bacterial + other organisms). Among the bacterial isolates Pseudomonas was the most common, followed by equally by Klebsiella and MRSA. This pattern is similar to the microbiological spectrum of Hospital acquired pneumonia where Gram negative organisms and MRSA are more common. These results are in accordance with several other published studies. [15,8] A similar study done by Rano et al [8]., showed the same results as our study. He observed in his study bacterial infections caused by MRSA and gram negative bacilli especially Pseudomonas were the most common cause of pulmonary infections. Since bacteria represent the most prevalent threat to immunocompromised patients, each institution should define the empirical antibiotic treatment based on its own data.

Tuberculosis was the second most common infectious cause (24% overall, TB alone 14% and TB + Others organisms 10%). In spite of excluding sputum AFB positive cases from the study, still the incidence of tuberculosis is quite high in our study. This highlights the importance of thoroughly searching for pulmonary tuberculosis among non-HIV immune compromised patients with pulmonary disease in high prevalence countries even if the sputum AFB smear is negative.

Jane C. Chan et al.,[27] in his study conducted in Hong Kong among 62 non-HIV immunocompromised patients found a similar result with tuberculosis being the second most common infection with a 19% incidence.

When compared with CBNAAT (gene Xpert) BAL AFB staining was able to detect only 53% of smear negative pulmonary tuberculosis cases in our study. Moreover, CBNAAT gives the added advantage of detecting Rifampicin resistance and the results are available within a few hours when compared to conventional culture which takes 8-12 weeks. Hence CBNAAT should be offered upfront to all non-HIV immunocompromised patients with pulmonary disease for diagnosis of pulmonary tuberculosis. In our study only 6% case of pulmonary tuberculosis was Rifampicin resistant, 7% showed indeterminate resistance and remaining 87% cases were rifampicin sensitive.

BAL fungal culture was positive in 23% (15 cases) in our study. But among fungal culture positive cases only 60% (9 cases) were diagnosed as proven or possible fungal infections requiring antifungal treatment as per the EORTC diagnostic criteria. In remaining 40% (6 cases) the isolated fungi from BAL culture could not be attributed to causing pulmonary disease as per diagnostic

criteria. These fungi might have colonized in the tracheobronchial tree without producing pulmonary lesions.

Among 6 patients in whom fungi were considered as colonizers 3 patients had co-infection with tuberculosis and one patient with bacteria for which they received treatment. In remaining 2 patients no other co-infection could be identified. From a CKD patient Candida tropicalis was isolated in culture and Candida albicans was isolated in BAL in AML patient. The significance of these colonizers fungi is not fully understood. Some studies have shown poor clinical outcomes in respiratory tract Candida colonization and is independently associated with increased hospital mortality [22,23].

Aspergillus species was the most common fungi isolated from respiratory tract of non-HIV immunocompromised patients in our study. Among Aspergillus species Niger was the most common, followed by Fumigatus.

Similar studies [15,8, 33] done in Non HIV immunocompromised patients show that among fungal infections Aspergillus is most common similar to our study.

Bacterial infections were more common among Renal Transplant Recipients (67%) & Fungal infections were more common among hematological malignancy (38%) patients and Tuberculosis was more common among CTD (38%) patients followed by CKD (31%) group.

NON-INFECTIOUS CAUSES OF PULMONARY INFILTRATES

In our study, 15% of pulmonary infiltrates were due to non-infectious causes. Among them most common cause (9%) was malignancy diagnosed by cytology or endobronchial biopsy and the remaining (6%) were due to radiation fibrosis, alveolar hemorrhage, interstitial pneumonia & lymphomatous infiltration of the lung in a case of secondary pulmonary lymphoma.

COMPLICATIONS OF BRONCHOSCOPY

Complications of bronchoscopy in our study were only minor except one case of pneumothorax which required ICD insertion. The overall complication rate was 24%. Transient hypoxemia during and within the first hour of bronchoscopy, which required supplemental oxygen occurred in 15%, followed by mild to moderate bleeding episodes during biopsy procedures occurred in 8%. Bleeding controlled by wedging the bronchoscope at the site of bleeding and cold saline instillation. Pneumothorax occurred in 1%.

Similar studies have shown the complication rate among non-HIV immunocompromised patients ranging from 13%-21%. [15,58] But complications were only minor in our study. But overall the complication rate of bronchoscopy is higher in immunocompromised patients. In general population, studies have shown the complication rate ranging widely from 5%-32%, with serious complication in 1.1% and mortality of 0.02% [45,60, 61]. There was no procedure related mortality in our study. Hence the proper pre procedural evaluation, patient selection and monitoring & care during/post procedure is necessary.

TREATMENT MODIFICATION & CLINICAL IMPROVEMENT

In our study empirical treatment was modified to the most appropriate treatment in 57% of patients based on bronchoscopic results which was statistically significant with P value 0.000 Studies have shown similar results like our study where treatment modification based on bronchoscopic yield has ranged from 38%-51%. [59,62,63] The treatment modification rate was higher in our study compared to other studies.

Among patients in whom treatment was modified, those in whom antibiotic were changed as per culture sensitivity pattern showed maximum clinical improvement with 90%, followed by those in whom anti tuberculosis treatment was started showed 70% improvement and those in whom antifungals were started 60% clinical improvement. Those patients in whom malignancy was diagnosed and second line chemotherapeutic agents restarted only 20% showed clinical improvement probably because of their advanced nature of the disease. The overall clinical improvement with treatment modification was around 70%.

SALIENT POINTS OBSERVED AMONG CANCER CHEMOTHERAPY PATIENTS IN OUR STUDY

- Pulmonary disease in this group was more commonly due to non-infectious etiology that is malignancy.
- Because of their non-infectious nature presence of fever at the time of presentation was lower, most patients had longer duration of symptoms.
- The nodular pattern was a most common radiological pattern.

- The clinical improvement with treatment modification was low.
- Bleeding was the most common complication which could be explained because of increased endobronchial biopsy done to achieve a diagnosis

SALIENT POINTS IN POSTRENAL TRANSPLANT GROUP IN OUR STUDY

- Fever was the predominant presenting symptom, most patients had acute symptoms at time of presentation
- Overall Bacterial infections were more common
- Immediate post-transplant period, bacterial infections were more, TB & fungal infections were more common after prolonged immunosuppression > 6 months
- Overall clinical improvement with change in treatment is good
- Transient hypoxemia during bronchoscopy was frequently encountered

SALIENT FINDINGS IN CKD GROUP

- Chest symptoms and hemoptysis are more common. Presence of fever is less in this group
- Most patients had acute presentation.
- Consolidation was a predominant radiological pattern
- Tuberculosis & bacterial infections are equally common.
- 75% of patients in whom treatment modified improved.
- Like post-transplant group hypoxemia was frequently encountered complication during the procedure

SALIENT FEATURES OF HAEMATOLOGICAL MALIGNANCY GROUP

- Chest symptoms followed by fever are most common presenting symptoms.
- Fungal infections are more predominant in this group.
- 50% of patients, treatment was modified based on bronchoscopic results and all patients in whom treatment modified improved.
- The overall complication rate is low if patients are properly worked up before the procedure like BT, CT, PT, a PTT, Platelet counts etc.

SALIENT FEATURES OF CTD GROUP

- Presence of fever at the time of initial presentation was less. This was probably because of the high level of immune suppression induced by drugs.
- In radiology reticular pattern was the most common presentation & because of the presence of underlying pulmonary interstitial involvement due to primary disease process per se.
- Diffuse pattern in radiological presentation was more common.
- Bacterial infection followed by tuberculosis were the common infective aetiologies.
- Out of 3 patients who were started on biological agents 2 developed tuberculosis.
- Bronchoscopy led to change in current treatment plan in 57%, out of which 75% improved clinically.
- Complications were low, bronchoscopy was safe and well tolerated.

CONCLUSION

- In our study, among Non-HIV immunocompromised patients with pulmonary diseases, we found Bronchoscopy as an useful tool. The yield of bronchoscopy was high (80%) despite empirical antimicrobial therapy.
- Out of positive bronchoscopic yield, 65% were due to infectious cause and 15% had non-infectious etiology. If bronchoscopy had not been performed, non-infectious cause could have been easily missed and treated as infectious.
- Among the infectious causes bacterial infections were the predominant cause of pulmonary disease (35% overall). Gram negative bacteria followed by MRSA were most common among the bacterial infections.
- Since Tuberculosis was second most common infectious cause (24% overall) it has to be ruled out in all non-HIV immunocompromised patients with pulmonary diseases in high prevalence countries.
- CBNAAT led to increased detection of tuberculous infection in our study when compared to BAL AFB staining. Hence genotypic test should be offered to all non-HIV immunocompromised for diagnosis of tuberculosis.
- Even though fungal infections were common among immunocompromised (23 % overall), we could attribute only 2/3rd as proven or probable fungal infections and remaining 1/3rd were colonizers.
- Presence of fever, alveolar & a focal pattern of infiltrates, upper lobe involvement increased the infectious yield of bronchoscopy.

- Overall bacterial infections were more common among renal transplant group, fungal infections among hematological malignancy group and tuberculosis was more common connective tissue group followed by CKD group.
- Complications of bronchoscopy in our study were only minor. Proper pre-procedure evaluation and patient selection and monitoring during the procedure reduced the complication rate.
- The current empirical treatment was modified to the most appropriate treatment in 57% who underwent bronchoscopy. Among the treatment modified group, 70% improved clinically.
- For clinically stable patients early bronchoscopy before starting empirical treatment can be the preferred approach. Patients who are clinically unstable or not fit for procedure, early empirical treatment is advised, followed by bronchoscopy once the general conditions improve or if the patient does not respond to empirical therapy**.**
- In summary, bronchoscopy among Non-HIV immune compromised patients was a safe procedure with good diagnostic yield and therapeutic utility. Hence, when encountered with a non-HIV immune compromised patient with pulmonary disease, early bronchoscopy must be preferred, as the benefits outweighs the risk.

LIMITATIONS

- The sample size of the study was small, and the sample size was not distributed equally among all groups.
- Methods to detect respiratory viruses and certain atypical microbes like Mycoplasma from BAL sample was included in the study methodology.
- Since sputum AFB positive cases were excluded from the study the overall incidence of tuberculosis may be underestimated in Non-HIV immunocompromised patients.
- Very sick patients and patients with an unstable general condition were excluded from the study.
- This study was done at a specialized tertiary care hospital and hence may not reflect the pattern of infection among non-HIV immunocompromised patients at community level. So further large scale studies are needed among non-HIV immunocompromised patients.

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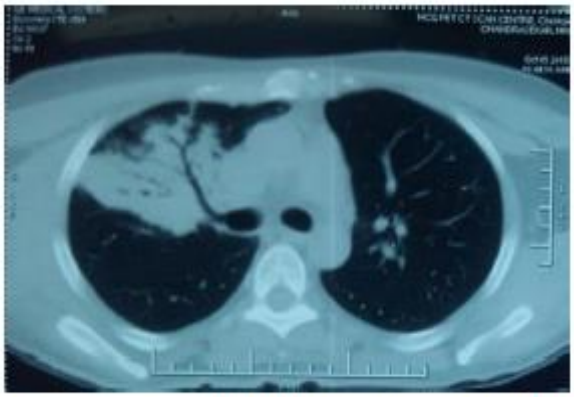
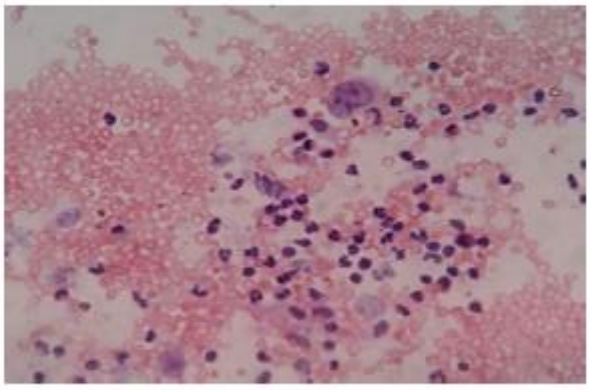
ANNEXURES – 1

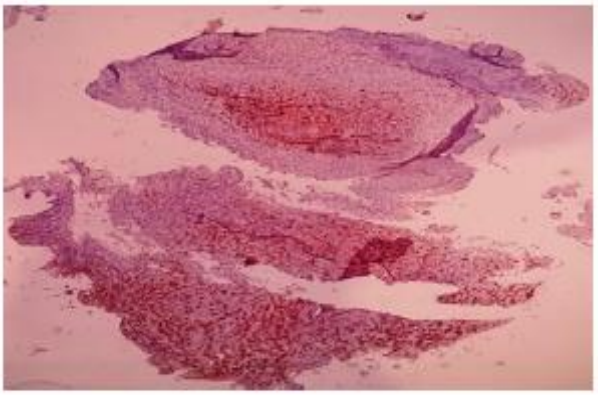
A CASE OF RIGHT UPPER LOBE CONSOLIDATION IN A PATIENT WITH HODGKINS LYMPHOMA ON CHEMOTHERAPY – FOB PROVED IT AS NON-INFECTIVE CONSOLIDATION



A) CT-CHEST SHOWING RIGHT UPPER LOBE CONSOLIDATION WITH AIR BRONCHOGRAM SIGN.



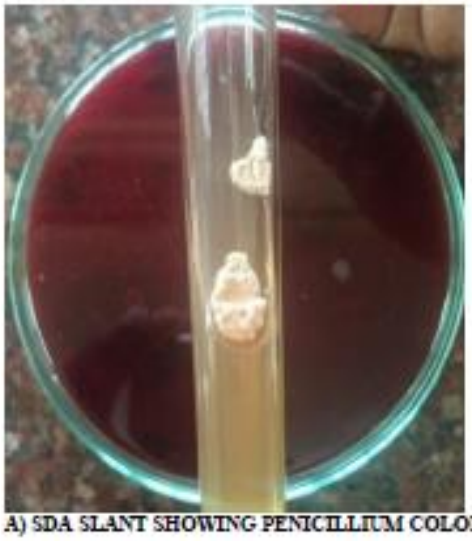
B) REED STERNG BERG CELLS IN BRONCHIAL WASH



c) IHC MARKERS FROM TBLB SHOWING CD 30 & CD 15 POSITIVITY

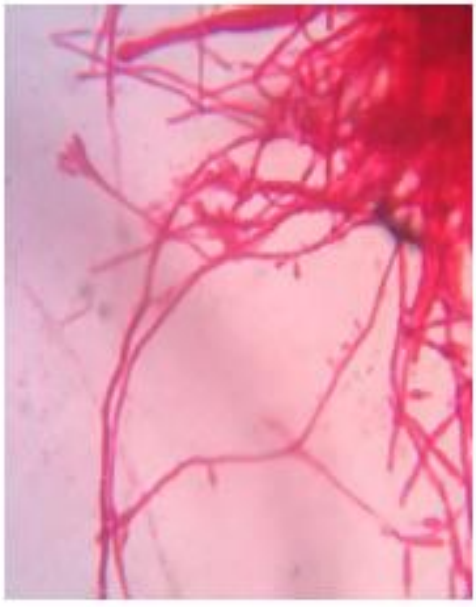
ANNEXURE – 2

A RARE CASE OF INVASIVE PENICILLUM MARNEFFI INFECTTION IN CKD PATIENT SUSPECTED TO HAVE TUBERCULOSIS

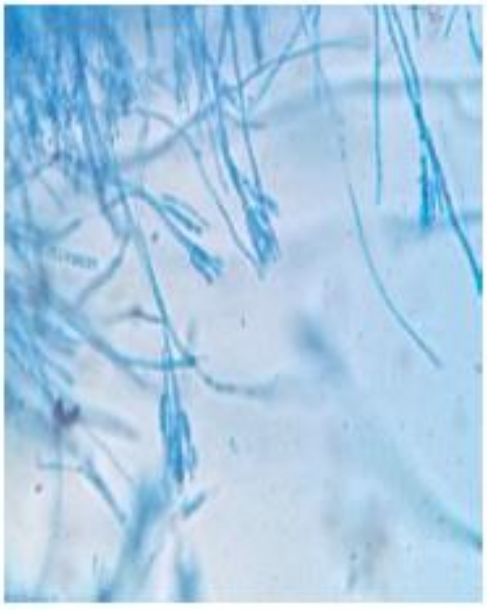


A) SDA SLANT SHOWING PENICILLIUM COLONIES

B) SDA PLATE SHOWING PENICILLIUM COLONIES IN BLOOD CULTURE



C) GRAMS STAIN SHOWING EARLY CONIDIA



D) LACTO PHENOL COTTON BLUE SHOWING CONIDIA.

ABBREVIATIONS

HIV – HUMAN IMMUNODEFICIENCY VIRUS

BMT – BONE MARROW TRANSPLANT

SOT – SOLID ORGAN TRANSPLANT

BAL – BRONCHO ALVEOLAR LAVAGE

CDC – CENTER FOR DISEASE CONTROL

IDSA – INFECTIOUS DISEASE OF AMERICA

HSCT – HAEMATOPOIETIC STEM CELL TRANSPLANT

CMV – CYTOMEGALO VIRUS

RSV – RESPIRATORY SYNCYTIAL VIRUS

CLL – CHRONIC LYMPHOCYTIC LEUKEMIA

PCP – PNEUMOCYTIS CARINI PNEUMONIA

MTB – MYCOBSCTERIUM TUBERCULOSIS

DAH – DIFFUSE ALVEOLAR HAEMORRHAGE

DAD – DIFFUSE ALVEOLAR DAMAGE

PBS – PROTECTED BRUSH SAMPLING

TBLB – TRANS BRONCHIAL BIOPSY

FOB – FIBER OPTIC BRONCHOSCOPY

GGO – GROUND GLASS OPACITY

BT – BLEEDING TIME, CT – CLOTTING TIME

PT – PROTHROMBIN TIME, APTT- ACTIVATED PARTIAL THROMBOPLASTIN TIME

EORTC - **E**UROPEAN **O**RGANIZATION FOR **R**ESEARCH AND **T**REATMENT OF CANCER/INVASIVE FUNGAL INFECTIONS **C**OOPERATIVE GROUP

ICD – INTER COSTAL DRAIN

CKD – CHRONIC KIDNEY DISEASE

CTD – CONNECTIVE TISSUE DISEASE

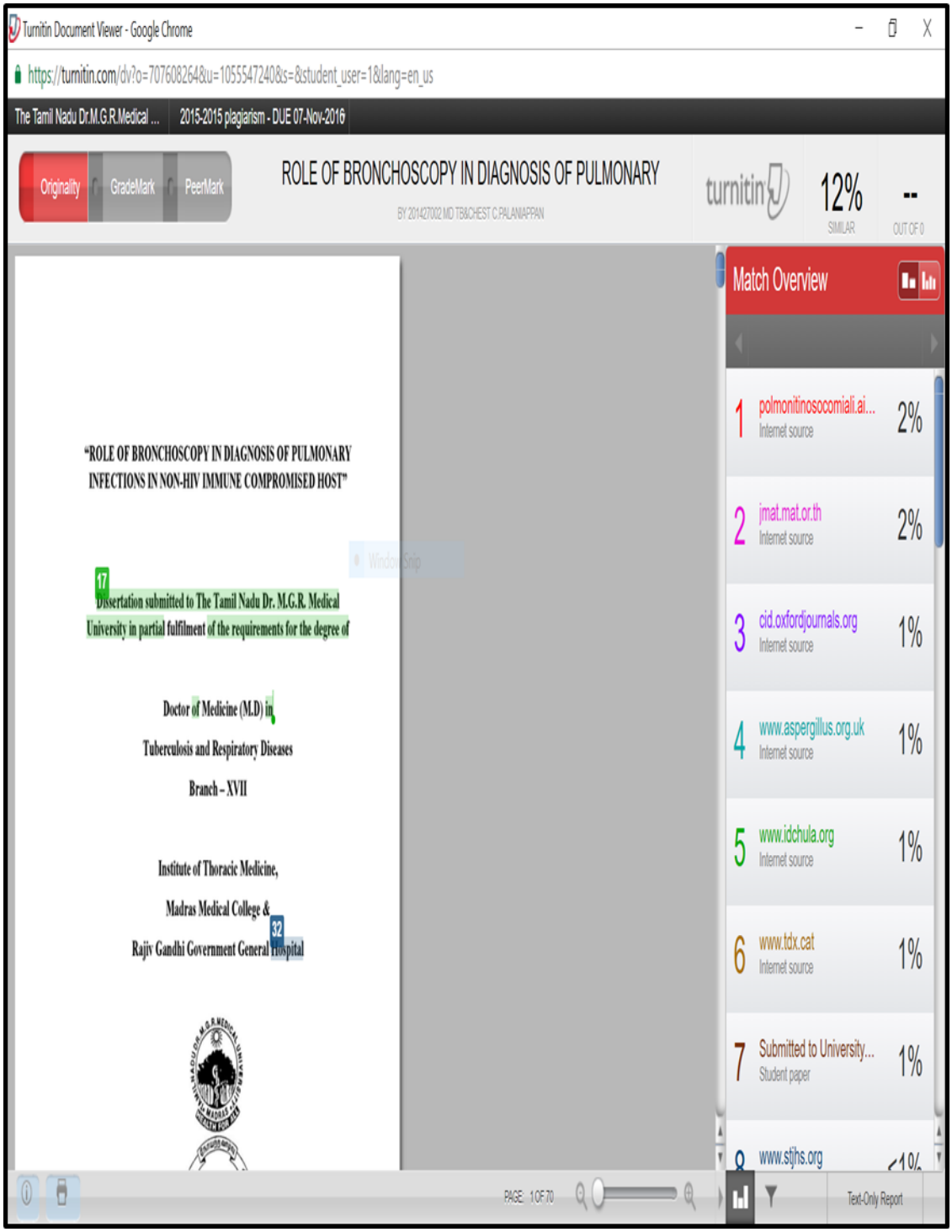
MRSA – METHICILLIN RESISTANT STAPHLYOCOCCUS AUREUS

TGB – THIOGLYCOLATE BROTH

SDA – SABURODS DEXTROSE AGAR

BA – BLOOD AGAR

PLAGIARISM SCREEN SHOT



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"ROLE OF BRONCHOSCOPY IN DIAGNOSIS OF PULMONARY INFECTIONS IN NON-HIV IMMUNE COMPROMISED HOST"

Dissertation submitted to The Tamil Nadu Dr. M.G.R. Medical University in partial fulfillment of the requirements for the degree of

Doctor of Medicine (M.D.) in

Tuberculosis and Respiratory Diseases

Branch – XVII

Institute of Thoracic Medicine,

Madras Medical College &

Rajiv Gandhi Government General Hospital

The Tamil Nadu Dr. M.G.R. Medical University

Chennai – 600032

Tamil Nadu

India

April 2017

ETHICAL COMMITTEE APPROVAL ORDER

MADRAS MEDICAL COLLEGE, CHENNAI 600 003

EC Reg.No.ECR/270/Inst./TN/2013
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CERTIFICATE OF APPROVAL

To
Dr.C.Palaniappan
PG in M.D.(TB & CD)
Madras Medical College/RGGGH
Chennai 600 003

Dear Dr.C.Palaniappan,

The Institutional Ethics Committee has considered your request and approved your study titled **" ROLE OF FIBRE OPTIC BRONCHOSCOPY IN DIAGNOSIS OF PULMONARY INFECTIONS IN NON HIV IMMUNE COMPROMISED HOST" - NO.10012016.**

The following members of Ethics Committee were present in the meeting hold on **12.01.2016** conducted at Madras Medical College, Chennai 3

1.Dr.C.Rajendran, MD.,	:Chairperson
2.Dr.R.Vimala,MD.,Dean,MMC,Ch-3	:Deputy Chairperson
3.Prof.Sudha Seshayyan,MD., Vice Principal,MMC,Ch-3	: Member Secretary
4.Prof.B.Vasanthi,MD.,Inst.of Pharmacology,MMC,Ch-3	: Member
5.Prof.P.Raghumani,MS, Dept.of Surgery,RGGGH,Ch-3	: Member
6.Prof.M.Saraswathi,MD.,Director, Inst.of Path,MMC,Ch-3	: Member
7.Tmt.J.Rajalakshmi, JAO,MMC, Ch-3	: Lay Person
8.Thiru S.Govindasamy, BA.,BL,High Court,Chennai	: Lawyer
9.Tmt.Arnold Saulina, MA.,MSW.,	:Social Scientist

We approve the proposal to be conducted in its presented form.

The Institutional Ethics Committee expects to be informed about the progress of the study and SAE occurring in the course of the study, any changes in the protocol and patients information/informed consent and asks to be provided a copy of the final report.

MADRAS MEDICAL COLLEGE
21 JAN 2016
CHENNAI-600 003

Member Secretary - Ethics Committee
MEMBER SECRETARY
INSTITUTIONAL ETHICS COMMITTEE
MADRAS MEDICAL COLLEGE
CHENNAI-600 003

TAMIL CONSENT FORM

ஆராய்ச்சி தகவல் தாள்

ஆராய்ச்சி தலைப்பு

எச்.ஐ.வி. அல்லாத நோய் எதிர்ப்பு திறன் குறைவாக உள்ளவர்களுக்கு நுரையீரலில் ஏற்படும் நோய் கிருமி தொற்றுக்கு காரணம் கண்டறிய மூச்சுக்குழாய் உள்நோக்கி கருவியின் பங்களிப்பு

ஆராய்ச்சியாளர் பெயர் : மருத்துவர்.சொ.பழனியப்பன்

பங்கேற்பாளர் பெயர் :

ஆராய்ச்சியின் நோக்கம்

எச்.ஐ.வி. நோய் அல்லாமல் பிற காரணங்களால் நோய் எதிர்ப்பு திறன் குறைவாக உள்ளவர்களுக்கு நுரையீரலில் ஏற்படும் நோய் கிருமி தொற்றுக்கு காரணம் அறிவதில் மூச்சுக்குழாய் உள்நோக்கு கருவியின் பங்களிப்பு பற்றி கண்டறிதல்.

இதன் மூலம் நோய் எதிர்ப்பு திறன் குறைவாக உள்ளவர்களுக்கு ஏற்படும் நுரையீரல் தொற்று கிருமிகளை விரைவாக கண்டறிந்து சரியான மற்றும் உரிய நேரத்தில் சிகிச்சை அளிக்க முடியும்.

ஆய்வு முறை

எச்.ஐ.வி. அல்லாத நோய் எதிர்ப்பு திறன் குறைவாக உள்ளவர்களில், நுரையீரலில் கிருமி தொற்று இருப்பதற்கு அறிகுறி உள்ளவர்கள் இந்த ஆய்வில் பங்குபெறுவர். அவர்களிடம் அவர்கள் நோய் சம்பந்தப்பட்ட வரலாறு முற்றிலுமாக கேட்டறியப்படும். அவர்களுக்கு நுரையீரல் மற்றும் இதர உறுப்புகள் சம்பந்தப்பட்ட மருத்துவ பரிசோதனை செய்யப்படும். நெஞ்சுப்படம் (எக்ஸ்-ரே) மற்றும் தேவைப்படும் நேரங்களில் சி.டி.ஸ்கேன் செய்யப்படும். தேவையான இரத்தப் பரிசோதனை செய்யப்படும். இருதயம் பரிசோதனை செய்யப்படும். மேலும், மூச்சுக்குழாய் உள்நோக்கி பரிசோதனை செய்யப்படும். சதை மாதிரிகள், சளி மாதிரிகள் எடுக்கப்பட்டு பரிசோதனை செய்யப்படும். மேலும் நோய் எதிர்ப்பு திறன்

குறைவாக உள்ளவர்களுக்கு ஏற்படும் நுரையீரலில் தொற்றுகளை கண்டறிவதில் தற்போது உள்ள மருத்துவ ஆராய்ச்சிகளின் படி மூச்சுக்குழாய் உள் நோக்கி பரிசோதனை மிகவும் பயனுள்ளதாகவும், அவசியமானதாகவும் கருதப்படுகிறது.

நன்மைகள்

இந்த பரிசோதனைகளின் முடிவுகளை வைத்து நோய்க்கான காரணம் கண்டறியப்பட்டு தக்க சிகிச்சை அளிக்க முடியும்.

இந்த முறையான ஆய்வு ஏற்கனவே பல இடங்களில் நடத்தப்பட்டுள்ளது. மேலும் இதன் பாதுகாப்பு உறுதிசெய்யப்பட்டுள்ளது. உங்கள் பாதுகாப்பே எங்களின் முக்கிய நோக்கம்.

இந்த ஆய்வு சம்பந்தமான எல்லா புள்ளி விவரங்கள் மற்றும் நோயாளிகளின் விவரங்கள் ரகசியமாக வைக்கப்படும். இந்த ஆய்வு சம்பந்தப்பட்ட எல்லா பரிசோதனைகள், மருந்துகள் மற்றும் மருத்துவ சேவைகள் அனைத்தும் நோயாளிகளுக்கு இலவசமாக வழங்கப்படும்.

ஆய்வாளரின் பெயர் பங்குபெறுபவரின் பெயர்

ஆய்வாளரின் கையொப்பம் பங்குபெறுபவரின் கையொப்பம்

PATIENT CONSENT FORM

Study Detail: **Role of Bronchoscopy in diagnosis of pulmonary infiltrates in non HIV immune compromised host.**

Study Centre: Rajiv Gandhi Government General Hospital, Chennai.

Patient's Name:

Patient's Age:

Identification

Number:

Patient may check (√) these boxes

a) I confirm that I have understood the purpose of procedure for the above study. I have the Opportunity to ask question and all my questions and doubts have been answered to my complete satisfaction. ❑

b) I understand that my participation in the study is voluntary and that I am free to withdraw at any time without giving reason, without my legal rights being affected.

❑

c) I understand that sponsor of the clinical study, others working on the sponsor's behalf, the ethical committee and the regulatory authorities will not need my permission to look at my health records, both in respect of current study and any further research that may be conducted in relation to it, even if I withdraw from the study I agree to this access. However, I understand that my identity will not be revealed in any information released to third parties or published, unless as required under the law. I agree not to restrict the use of any data or results that arise from this study. ❑

d) I agree to take part in the above study and to comply with the instructions given during the study and faithfully cooperate with the study team and to immediately inform the study staff if I suffer from any deterioration in my health or wellbeing or any unexpected or unusual symptoms. ❑

e) I hereby consent to participate in this study. ❑

f) I hereby give permission to undergo detailed clinical examination, Radiographs, blood Investigations and surgical procedure as required. ❑

Signature/thumb impression

Signature of Investigator

Patient name and address

Study investigators name:

[DR C. PALANIAPPAN]

PATIENT INFORMATION SHEET

TITLE OF THE STUDY: **Role of Bronchoscopy in diagnosis of pulmonary infiltrates in non HIV immune compromised host.**

We are conducting a study on among patients admitted in Rajiv Gandhi Government General Hospital, Chennai

The purpose of this study is to analyse **The Role of Bronchoscopy in diagnosis of pulmonary infiltrates in non HIV immune compromised host.**

We are selecting cases of immunocompromised patients who are HIV negative with persistent lung infiltrates in radiography despite antibiotic therapy as per the definition and the selected

Patients will undergo basic blood investigations, CT chest (if needed), fibre-optic bronchoscopy and CT guided Biopsy (if necessary) to arrive at a diagnosis and subsequently treat the patient.

The privacy of the patients in the research will be maintained throughout the study. In the event of any publication or presentation resulting from the research, no personally identifiable information will be shared.

Taking part in this study is voluntary. You are free to decide whether to participate in this study or to withdraw at any time; your decision will not result in any loss of benefits to which you are otherwise entitled.

The results of the special study may be intimated to you at the end of the study period or during the study if anything is found abnormal which may aid in the management or treatment.

Signature of investigator: Signature of participant

Date

EVALUATION FORM

Name:

Age:

Sex:

IP number:

Ward:

Presenting complaints:

History of presenting illness:

Past history:

Treatment history:

Personal history:

Occupational history:

General examination:

Systemic examination:

Blood investigations:

Radiological findings:

Chest x-ray:

CT-CHEST:

Sputum investigations:

Bronchoscopy findings and investigation results:

Transbronchial/Endobronchial biopsy reports:

Final diagnosis:

MASTER CHART

S.NO	NAME	AGE	SEX	DIAGNOSIS CA=1 RENAL TRANSPLANT=2 CKD=3 HAEMATOLOGICAL MALIGNANCY =4 CTD=5	CA TYPES LUNG=1 STOMACH=2 ESOPHAGUS=3 PHARYNX=4 BREAST=5	AUTOIMMUNE DISEASES SLE=1 RA=2 SCL=3 SJOG=4	HAEMATOLOGICAL MALIGNANCY HL=1 NHL=2 AML=3
1	JAYABALAN	59	M	1	1	0	0
2	CHELLAMUTHU	61	M	2	0	0	0
3	RAJATHI	32	F	5	0	1	0
4	RAVICHANDRAN	59	M	2	0	0	0
5	CHANDRABHAVANI	52	F	2	0	0	0
6	GHANSHEKAR	61	M	3	0	0	0
7	PRAKASAM	53	M	2	0	0	0
8	KUMAR	45	M	1	2	0	0
9	VELAYUTHAM	66	M	1	2	0	0
10	SUBAHVA	30	F	1	5	0	0
11	PATCHAYAMMA	50	F	5	0	2	0
12	SENTHILKUMAR	38	M	2	0	0	0
13	ANANDAN	44	M	2	0	0	0
14	MANOHARAN	26	M	2	0	0	0
15	SATHYA	21	F	5	0	2	0
16	MANIKANDAN	38	M	4	0	0	1
17	CHANDRASEKAR	31	M	4	0	0	1
18	RAJENDRAN	48	M	1	4	0	0
19	MICHEAL JEYARAJ	64	M	4	0	0	2
20	RAMESH	28	M	2	0	0	0
21	RASHUL	30	M	4	0	0	1
22	POOJA	17	F	5	0	1	0
23	JEYACHANDRAN	67	M	4	0	0	3
24	USHA	32	F	5	0	2	0
25	SHANTHI	65	F	5	0	1	0
26	VENKATARATHNAM	63	F	5	0	2	0
27	LOGANATHAN	27	M	2	0	0	0
28	MAHALAKSHMI	35	F	5	0	1	0
29	ERIBHAN	57	M	1	4	0	0
30	BALAJI	33	M	2	0	0	0
31	DEVAMMAL	69	F	5	0	1	0
32	KAVITHA	28	F	2	0	0	0
33	AYYAMMAL	69	F	1	5	0	0

S NO	NAME	AGE	SEX	DIAGNOSIS CA=1 RENAL TRANSPLANT=2 CKD=3 HAEMATOLOGICAL MALIGNANCY =4 CTD=5	CA TYPES LUNG=1 STOMACH=2 OESOPHAGUS=3 PHARYNX=4 BREAST=5	AUTOIMMUNE DISEASES SLE=1 RA=2 SCL=3 SJOG=4	HAEMATOLOGICAL MALIGNANCY HL=1 NHL=2 AML=3
34	GEETHA	31	F	5	0	3	0
35	KARTHIKEYAN	39	M	3	0	0	0
36	DEEPA	37	F	5	0	2	0
37	KRISHNAMOORTHY	35	M	3	0	0	0
38	CHITRA	31	F	3	0	0	0
39	PARTHASARATHY	37	M	3	0	0	0
40	GAUHAR SHAKIR	62	F	5	0	4	0
41	ANNADURAI	41	M	1	4	0	0
42	SUMITRA	35	F	2	0	0	0
43	LEEYA	32	F	5	0	3	0
44	RAVEENDRAN	56	M	3	0	0	0
45	ABHAYA	36	F	3	0	0	0
46	BALAJI	30	M	3	0	0	0
47	PERUMAL	54	M	5	0	2	0
48	LATHA	48	F	5	0	2	0
49	BIMAL	33	M	3	0	0	0
50	MUNIAPPAN	39	M	2	0	0	0
51	MURUGAN	50	M	3	0	0	0
52	DHANAPAL	62	M	1	4	0	0
53	VENIA	25	F	5	0	0	0
54	PUNNIYAKODI	30	M	2	0	0	0
55	VARADHARAJAN	65	M	1	4	0	0
56	CHANDRA	55	F	1	5	0	0
57	VIJAY	20	M	4	0	0	3
58	REMIKA	25	F	4	0	0	3
59	MALA	62	F	5	0	4	0
60	RUBANLAL	65	M	4	0	0	3
61	THILAGI	35	F	5	0	1	0
62	JEYANTHI	40	F	5	0	3	0
63	KALAVATHY	50	F	5	0	3	0
64	MENAKA	25	F	5	0	2	0
65	RAJESH	25	M	2	0	0	0

S NO	NAME	IMMUNOSUPPRESSION CHEMOTHERAPY=1 IMMUNOSUPPRESSANTS=2 STEROIDS=3 BIOLOGICALS=4 CKD=5 HAEMATOLOGICAL=6	RENAL TRANSPLANT DURATION 1=<1 M 2=1-6 M 3=> 6M	SYMPTOMS CHEST SYMPTOMS/FEVER=1 CHEST SYMPTOMS=2 HAEMOPTYSIS=3 FEVER=4 ASYMPTOMATIC=5	DURATION 0=ASYMPTOMATIC 1=0-3 WEEKS 2=3-8 WEEKS 3=>8 WEEKS	RADIOLOGY CONSOLIDATION=1 GGO=2 TREE IN BUD=3 NODULAR=4 RETICULAR=5 CAVITY=6
1	JAYAPALAN	1	0	1	3	1
2	CHELLAMUTHU	2	3	1	1	2
3	RAJATHI	3	0	2	1	1
4	RAVICHANDRAN	5	0	2	1	2
5	CHANDRABHAVADI	2	3	1	1	2
6	GNANASEKAR	5	0	1	2	2
7	PRAKASAM	2	1	1	1	3
8	KUMAR	1	0	2	2	4
9	VELAYUTHUM	1	0	3	3	1
10	SUGANYA	1	0	2	3	1
11	PATCHAYAMMA	2	0	2	1	5
12	SENTHILKUMAR	2	3	1	1	1
13	ANANDAN	5	3	2	1	1
14	MANIMARAN	5	0	2	1	1
15	SATHYA	3	0	1	1	5
16	MASILAMANI	1	0	5	0	5
17	CHANDRASEKAR	1	0	2	2	1
18	RAJENDRAN	1	0	2	2	4
19	MICHEAL JEYARAJ	1	0	2	3	4
20	RAMESH	2	1	2	1	1
21	RAGHUL	6	0	2	2	2
22	POOJA	2	0	1	2	1
23	JEYACHANDRAN	6	0	2	1	1
24	UMA	4	0	2	2	6
25	SHANTHI	3	0	2	1	2
26	VENKATARATHNAM	4	0	4	1	2
27	LOGANATHAN	5	0	1	1	1
28	MAHALAKSHMI	3	0	2	2	3
29	KRISHNAN	1	0	2	2	4
30	PALANI	5	0	2	1	1
31	DEVAMMAL	3	0	3	1	6
32	KAVITHA	5	0	2	2	1
33	AYYAMMAL	1	0	2	3	6

S NO	NAME	IMMUNOSUPPRESSION CHEMOTHERAPY=1 IMMUNOSUPPRESANTS=2 STEROIDS=3 BIOLOGICALS=4 CKD=5 HAEMATOLOGICAL=6	RENAL TRANSPLANT DURATION 1=<1 M 2=> 1-6 M 3=> 6 M	SYMPTOMS CHEST SYMPTOMS/FEVER =1 CHEST SYMPTOMS=2 HAEMOPTYSIS=3 FEVER=4 ASYMPTOMATIC=5	DURATION 1=ASYMPTOMATIC 1=0-3 WEEKS 2=3-8WEEKS 3=>8 WEEKS	RADIOLOGY CONSOLIDATION=1 GGO=2 TREE IN BUD=3 NODULAR=4 RETICULAR=5 CAVITY=6
34	GEETHA	2	0	2	3	5
35	KARTHIKEYAN	5	0	2	2	2
36	DEEPA	3	0	2	1	1
37	KRISHNAMOORTHY	5	0	3	1	1
38	CHITRA	5	0	2	2	3
39	PARTHASARATHY	5	0	3	1	1
40	GAUHAR SHAKIR	3	0	2	1	6
41	ANNADURAI	1	0	4	1	1
42	SUMITHRA	2	2	2	1	1
43	LEKHA	4	0	2	1	5
44	RAVEENDRAN	5	0	3	1	1
45	ARNAYA	5	0	3	1	1
46	BALAJI	5	0	2	2	1
47	PERUMAL	3	0	2	1	1
48	LATHA	3	0	2	2	1
49	ISMAIL	2	0	2	2	1
50	MUNIAPPAN	2	3	4	1	1
51	MURUGAN	5	0	2	1	1
52	DHANAPAL	1	0	3	1	6
53	VIDHYA	2	0	3	1	2
54	PUNNIYAKODI	2	2	3	2	1
55	VARADHARAJAN	1	0	2	3	1
56	CHANDRA	1	0	1	2	4
57	VIJAY	6	0	4	1	6
58	RENUKA	6	0	4	1	6
59	MALA	3	0	2	3	3
60	ELUMALAI	1	0	5	0	4
61	THILAGI	2	0	1	2	5
62	JEYANTHI	2	0	2	2	5
63	KALAVATHY	3	0	5	0	5
64	MINAKA	3	0	2	2	1
65	RAJESH	2	1	4	1	1

S NO	NAME	LOBES UPPER LOBE=1 MIDDLE LOBE/LINGULA =2 LOWER LOBE=3	LOBES FOCAL=1 DIFFUSE=2	GRAMS STAIN POSITIVE=1 NEGATIVE=2	AFB STAIN POSITIVE=1 NEGATIVE=2	GENE XPERT DETECTED=1 NOT DETECTED=2	RIF SENSITIVITY SENSITIVE=1 RESISTANT=2 INDETERMINATE =3	TUBERCULOSIS POSITIVE=1 NEGATIVE=2
1	JAYAPALAN	3	1	1	2	1	1	1
2	CHELLAMUTHU	3	1	1	2	1	1	1
3	RAJATHI	2	1	1	2	2	0	2
4	RAVICHANDRAN	3	2	2	2	2	0	2
5	CHANDRABHAVANI	2	2	1	2	2	0	2
6	GNANASEKAR	3	1	1	2	2	0	2
7	PRAKASAM	3	2	1	2	2	0	2
8	KUMAR	2	2	2	2	2	0	2
9	VELAYUTHUM	3	1	1	2	2	0	2
10	SUGANYA	2	1	2	2	2	0	2
11	PATCHAYAMMA	3	2	2	2	1	1	1
12	SENTHILKUMAR	3	1	1	2	2	0	2
13	ANANDAN	3	1	2	2	2	0	2
14	MANIMARAN	2	1	2	2	2	0	2
15	SATHYA	3	2	2	2	2	0	2
16	MAILAMANI	3	1	2	2	2	0	2
17	CHANDRASEKAR	1	1	2	2	2	0	2
18	RAJENDRAN	2	2	2	2	2	0	2
19	MICHAELJEYARAJ	2	2	1	2	1	1	1
20	RAMESH	1	1	1	2	2	0	2
21	RAGHUL	1	1	2	2	2	0	2
22	POOJA	2	1	1	2	2	0	2
23	JEYACHANDRAN	1	1	2	2	2	0	2
24	UMA	1	1	2	1	1	1	1
25	SHANTHI	3	2	2	1	1	1	1
26	VENKATARATHNAM	3	2	2	2	2	0	2
27	LOGANATHAN	3	1	1	2	2	0	2
28	MAHALAKSHMI	3	2	1	2	2	0	2
29	KRISHNAN	3	1	2	2	2	0	2
30	PALANI	3	1	2	2	2	0	2
31	DEVAMMAL	2	1	1	1	1	0	1
32	KAVITHA	2	1	1	2	2	0	2
33	AYYAMMAL	2	1	1	2	2	0	2

S NO	NAME	LOBES UPPER LOBE=1 MIDDLE LOBE/LINGULA =2 LOWER LOBE=3	LOBES FOCAL=1 DIFFUSE=2	GRAMS STAIN POSITIVE=1 NEGATIVE=2	AFB STAIN POSITIVE=1 NEGATIVE=2	GENE XPERT DETECTED=1 NOT DETECTED=2	RIF SENSITIVITY SENSITIVE=1 RESISTANT=2 INDETERMINATE =3	TUBERCULOSIS POSITIVE=1 NEGATIVE=2
34	GEETHA	2	2	1	2	2	0	2
35	KARTHIKEYAN	3	2	2	2	2	0	2
36	DEEPA	1	1	1	1	1	1	1
37	KRISHNAMOORTHY	2	1	2	2	2	0	2
38	CHITRA	1	1	2	2	1	2	1
39	PARTHASARATHY	3	1	1	2	1	3	1
40	GAUHAR SHAKIR	1	1	1	1	1	1	1
41	ANNADURAI	1	1	2	2	2	0	2
42	SUMITRA	1	1	2	2	2	0	2
43	LEKHA	3	2	2	2	1	1	1
44	RAVEENDRAN	1	1	2	1	1	1	1
45	ARUNATA	3	1	2	1	1	1	1
46	RAJAJI	2	1	2	2	1	1	1
47	PERUMAL	1	1	2	2	2	0	2
48	LATHA	1	1	1	2	2	0	2
49	ISMAIL	1	1	1	2	2	0	2
50	MUNIAPPAN	3	1	1	2	2	0	2
51	MURUGAN	1	1	1	2	2	0	2
52	DHANAPAL	3	1	2	2	2	0	2
53	VIDHYA	1	1	2	2	2	0	2
54	PUNNYAKODI	3	2	1	2	2	0	2
55	VARADHARAJAN	1	1	2	2	2	0	2
56	CHANDRA	1	1	2	2	2	0	2
57	VIJAY	1	1	1	2	2	0	2
58	RENUKA	1	1	1	2	2	0	2
59	MALA	2	1	2	1	2	0	2
60	KUMALAI	2	1	2	2	2	0	2
61	THILAGI	3	2	2	2	2	0	2
62	JEYANTHI	3	2	2	2	2	0	2
63	KALAVATHY	3	2	2	2	2	0	2
64	MENAKA	2	1	2	1	1	1	1
65	RAJESH	1	1	2	2	2	0	2

S.NO	NAME	BACTERIAL CULTURE POSITIVE=1 NEGATIVE=2	BACTERIAL CULTURE NIL=0 KLEBSIELLA=1 PSEUDOMONAS=2 ACINETOBACTER=3 STEPP PNEUMONIA=4 ENTEROCOCCI=5 MRSA=6 ECOLI=7 PSEUDOMONAS+MRSA=8	FUNGAL CULTURE POSITIVE=1 NEGATIVE=2	FUNGAL CUL N=0 C.ALBICANS=1 C.PARAPSILPLOSIS=2 C.TROPICALIS=3 PENICILLIUM=4 A.NIGER=5 A.FUMIGATUS=6 A.FLAVUS=7 A.VERSICOLOR=8	YEELD POSITIVE=1 NEGATIVE=2	INFECTION/ NON-INFECTION 0=NIL INFECTION=1 NON-INFECTION=2	INFECTION/S 0=NIL/NI 1=TB 2=BACTERIAL 3=FUNGAL 4=MIXED
1	JAYAPALAN	2	0	2	0	1	1	1
2	CHELLAMUTHU	2	0	2	0	1	1	1
3	RAJATHI	1	2	2	0	1	1	2
4	RAVICHANDRAN	2	0	2	0	2	0	0
5	CHANDRABHAVANI	1	3	1	2	1	1	4
6	GNANASEKAR	2	0	1	4	1	1	3
7	PRAKASAM	1	3	2	0	1	1	2
8	KUMAR	2	0	2	0	1	2	0
9	VELAYUTHUM	1	4	2	0	1	1	2
10	SUGANYA	2	0	2	0	1	2	0
11	PANCHAVARNAM	2	0	2	0	1	1	1
12	SENTHILKUMAR	1	2	2	0	1	1	2
13	ANANDAN	2	0	1	3	1	1	3
14	MANIMARAN	2	0	2	0	2	0	0
15	SATHYA	2	0	2	0	1	2	0
16	MASILAMANI	2	0	2	0	2	0	0
17	CHANDRASEKAR	2	0	2	0	1	2	0
18	RAJENDRAN	2	0	2	0	1	2	0
19	MUNIRAJ.IYYARAJ	2	0	2	0	1	1	1
20	RAMESH	1	1	2	0	1	1	2
21	RACHEL	2	0	1	5	1	1	3
22	POOJA	1	8	2	0	1	1	2
23	JEYACHANDRAN	2	0	1	1	1	1	3
24	UMA	2	0	2	0	1	1	1
25	SHANTHI	2	0	2	0	1	1	1
26	VENKATARATHNAM	1	2	2	0	1	1	2
27	LOGANATHAN	1	5	2	0	1	1	2
28	MAHALAKSHMI	1	6	2	0	1	1	2
29	KRISHNAN	2	0	2	0	1	2	0
30	PALANI	2	0	2	0	2	0	0
31	DEIVAMMAL	1	7	2	0	1	1	4
32	KAVITHA	1	2	2	0	1	1	2
33	AYYAMMAL	2	2	1	5	1	1	3

S NO	NAME	BACTERIAL CULTURE POSITIVE=1 NEGATIVE=2	BACTERIAL CULTURE NIL=0 KLEBSIELLA=1 PSEUDOMONAS=2 ACINETOBACTER=3 STREP PNEUMONIA=4 ENTEROCOCCI=5 MRSA=6 ECOLI=7 PSEUDOMONAS+MRSA=8	FUNGAL CULTURE POSITIVE=1 NEGATIVE=2	FUNGAL CULTURE NIL=0 C.ALBICANS=1 C.PARAPSILOSIS=2 C.TROPICALIS=3 PENICILLIUM=4 A.NIGER=5 A.FUMIGATUS=6 A.FLAVUS=7 A.VERSICOLOR=8	YEELD POSITIVE=1 NEGATIVE=2	INFECTIONS NON. INFECTION 0=NIL INFECTION=1 NON. INFECTION=2	INFECTIONS 0=NIL/N1 1=TB 2=BACTERIAL 3=FUNGAL 4=MIXED
34	GEETHA	1	5	1	8	1	1	4
35	KARTHIKEYAN	2	0	2	0	2	0	0
36	DEEPA	1	6	2	0	1	1	4
37	KRISHNAMOORTHY	2	0	2	0	2	0	0
38	CHITRA	2	0	2	0	1	1	1
39	PARTHASARATHY	1	3	2	0	1	1	4
40	GAUHAR SHAKIR	1	2	1	6	1	1	4
41	ANNADURAI	2	0	1	6	1	1	3
42	SUMITHRA	2	0	2	0	1	0	0
43	LENYA	2	0	2	0	1	1	1
44	RAVEENDRAN	2	0	2	0	1	1	1
45	ABHAYA	2	0	1	7	1	1	4
46	BALAJI	2	0	1	7	1	1	4
47	PERUMAL	2	0	2	0	2	0	0
48	LATHA	1	6	2	0	1	1	2
49	ISMAIL	1	1	1	5	1	1	4
50	MUNIAPPAN	1	2	1	5	1	1	4
51	MURUGAN	1	1	2	0	1	1	2
52	DHANAPAL	2	0	2	0	1	2	0
53	VIDHYA	2	0	2	0	1	2	0
54	PUNNYAKODI	1	6	2	0	1	1	2
55	VARADHARAJAN	2	0	2	0	1	2	0
56	CHANDRA	2	0	2	0	1	2	0
57	VIJAY	1	1	2	0	1	1	2
58	RENUKA	2	0	1	6	1	1	3
59	MALA	2	0	2	0	2	0	0
60	ELUMALAI	2	0	2	0	2	0	0
61	THULASI	2	0	2	0	2	0	0
62	JEYANTHI	2	0	2	0	2	0	0
63	KALAVATHY	2	0	2	0	2	0	0
64	MENAKA	2	0	2	0	1	1	0
65	RAJESH	2	0	1	1	1	1	3

SNO	NAME	COMPLICATIONS NIL=0 HYPOXEMIA=1 BLEEDING=2 PNEUMOTHORAX=3	COMPLICATION YES=1 NO=2	TREATMENT MODIFIED YES=1 NO=2	TRT ATT=1 ANTIBIOTICS CHANGED=2 ANTIFUNGALS=3 UNCHANGED=4 CHEMOTHERAPY STARTED=5	FOLLOW IMPROVED=1 LOST=2 ON FOLLOE UP=3 DIED=4	FOLLOW UP IMPROVED=1 2=NON IMPROVED/DIED/LOST
1	JAYAPALAN	0	2	1	1	1	1
2	CHELLAMUTHU	1	1	1	1	1	1
3	RAJATHI	0	2	2	2	1	1
4	RAVICHANDRAN	0	2	2	4	1	1
5	CHANDRABHAVANI	1	1	1	2	1	1
6	GNANASEKAR	0	2	1	3	1	1
7	PRAKASAM	1	1	1	2	1	1
8	KUMAR	0	2	2	4	2	2
9	VELAYUTHUM	0	2	2	4	1	1
10	SUGANYA	0	2	2	4	1	1
11	PATCHAYAMMA	0	2	1	1	1	1
12	SENTHILKUMAR	1	1	1	2	1	1
13	ANANDAN	1	1	2	4	2	2
14	MANIMARAN	1	1	2	4	1	1
15	SATHYA	0	2	2	4	1	1
16	MASILAMANI	0	2	2	4	1	1
17	CHANDRASEKAR	0	2	1	5	1	1
18	RAJENDRAN	2	1	2	4	2	2
19	MUNIRAJ.JEYARAJ	0	2	1	1	1	1
20	RAMESH	0	2	2	4	1	1
21	RAGHUL	0	2	1	3	1	1
22	POOJA	3	1	1	2	1	1
23	JEYACHANDRAN	2	1	2	4	2	2
24	UMA	0	2	1	1	1	1
25	SHANTHI	0	2	1	1	1	1
26	VENKATARATHNAM	0	2	1	2	1	1
27	LOGANATHAN	1	1	1	2	1	1
28	MAHALAKSHMI	0	2	2	4	1	1
29	KRISHNAN	0	2	2	4	4	2
30	PALANI	2	1	2	4	1	1
31	DEIAMMAL	0	2	1	1	1	1
32	KAVITHA	0	2	1	2	4	2
33	ATYAMMAL	0	2	1	3	1	1

SNO	NAME	COMPLICATIONS NIL=0 HYPOXEMIA=1 BLEEDING=2 PNEUMOTHORAX=3	COMPLICATION YES=1 NO=2	TREATMENT MODIFIED YES=1 NO=2	TRT ATT=1 ANTIBIOTICS CHANGED=2 ANTIFUNGALS=3 UNCHANGED=4 CHEMOTHERAPY STARTED=5	FOLLOW IMPROVED=1 LOST=2 ON FOLLOE UP=3 DIED=4	FOLLOW UP IMPROVED=1 2=NON IMPROVED/DIED/LOST
34	GEETHA	0	2	1	3	2	2
35	KARTHIKEYAN	0	2	2	4	1	1
36	DEEPA	0	2	1	1	2	2
37	KRISHNAMOORTHY	0	2	2	4	1	1
38	CHITRA	0	2	1	1	3	2
39	PARTHASARATHY	1	1	1	1	1	1
40	GAUHAR SHAIKH	0	2	1	1	1	1
41	ANNADURAI	0	2	1	3	2	2
42	SUMITHRA	0	2	2	4	3	2
43	LENYA	0	2	1	1	1	1
44	RAVEENDRAN	0	2	1	1	4	2
45	ABINAYA	1	1	1	1	1	1
46	BALAJI	0	2	1	1	1	1
47	PERUMAL	0	2	2	4	1	1
48	LATHA	0	2	2	4	1	1
49	KAMAL	0	2	1	3	1	1
50	MUNIAPPAN	0	2	1	3	1	1
51	MURUGAN	0	2	2	4	1	1
52	DHANAPAL	2	1	1	5	3	2
53	VIDHYA	0	2	1	5	3	2
54	PUNNYAKODI	0	2	2	4	1	1
55	VARADHARAJAN	2	1	1	5	3	2
56	CHANDRA	0	2	1	5	4	2
57	VIJAY	0	2	2	4	1	1
58	RENUKA	0	2	1	3	1	1
59	MALA	0	2	2	4	1	1
60	ELUMALAI	0	2	2	4	1	1
61	THILASI	0	2	2	4	1	1
62	JEYANTHI	0	2	2	4	1	1
63	KALAVATHY	0	2	2	4	1	1
64	MENAKA	0	2	1	4	3	2
65	RAJESH	1	1	1	3	4	2